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L1: Entry 10 of 19 File: USPT Jul 30, 1996

US-PAT-NO: 5541098
DOCUMENT-IDENTIFIER: US 5541098 A

TITLE: Urate oxidase activity protein, recombinant gene coding therefor, expression vector, micro-organisms and transformed cells

DATE-ISSUED: July 30, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caput; Daniel	Toulouse			FR
Ferrara; Pascual	Vilefranche de Lauragais			FR
Guillemot; Jean-Claude	Toulouse			FR
Kaghad; Mourad	Ramonville St. Agne			FR
LeGoux; Richard	Caraman			FR
Loison; G erard	Toulouse			FR
Larbre; Elisabeth	Avignon			FR
Lupker; Johannes	Castanet-Tolosan			FR
Leplatois; Pascal	Cuq Toulza			FR
Salome; Marc	Castanet-Tolosan			FR
Laurent; Patrick	Pechbusque			FR

US-CL-CURRENT: 435/191; 435/252.33, 435/254.21, 435/320.1, 435/365, 536/23.2

CLAIMS:

What is claimed is:

1. An isolated, purified gene which comprises a polynucleotide encoding the protein of the sequence of SEQ ID NO:2.

2. An isolated, purified gene according to claim 1, which permits expression in prokaryotic microorganisms.

3. An isolated, purified gene according to claim 12, wherein the polynucleotide has the sequence of SEQ ID NO:3.

4. An isolated, purified gene according to claim 1, which permits expression in eukaryotic cells.

5. An isolated, purified gene according to claim 4, wherein the polynucleotide has the sequence of SEQ ID NO:4.

6. An isolated, purified gene according to claim 1, which permits expression in animal cells.

7. An isolated, purified gene according to claim 6, wherein the polynucleotide has the sequence of SEQ ID NO:6,

said gene further comprising a non-translated 5' polynucleotide upstream of said

polynucleotide that favors expression in animal cells.

8. An isolated, purified gene according to claim 7, wherein the non-translated 5' polynucleotide favoring expression in animal cells comprises the sequence AGCTTGCCGCCACT (SEQ ID NO:5), which is immediately upstream of said polynucleotide having the sequence of SEQ ID NO:6.

9. An expression vector which carries an isolated, purified gene according to claim 1 and the means necessary for its expression.

10. An expression vector which carries an isolated, purified gene according to claim 2 and the means necessary for its expression.

11. An expression vector which carries an isolated, purified gene according to claim 4 and the means necessary for its expression.

12. An expression vector which carries an isolated, purified gene according to claim 7 and the means necessary for its expression.

13. An expression vector according to claim 9, which carries at least one selection marker.

14. An expression vector according to claim 10, which carries at least one selection marker.

15. An expression vector according to claim 11, which carries at least one selection marker.

16. An expression vector according to claim 15, which has the characteristics of one of plasmids pEMR469, pEMR473, or pEMR515.

17. Prokaryotic microorganisms, which are transformed by an expression vector according to claim 10.

18. Eukaryotic cells, which are transformed by an expression vector according to claim 11.

19. Eukaryotic cells, which are transformed by an expression vector according to claim 15.

20. Eukaryotic cells, which are transformed by an expression vector according to claim 16.

21. An eukaryotic cell according to claim 19, which is a strain of S. cerevisiae.

22. A cell according to claim 21, which carries a mutation on at least one of the genes responsible for the synthesis of leucine or uracil.

23. A cell according to claim 22, which carries a mutation on at least one of the LEU2 and URA3 genes.

24. A process for producing recombinant urate oxidase which comprises the steps of:

1) cultivating a cell according to claim 21;

2) lysing the cells;

3) isolating and purifying the recombinant urate oxidase contained in the lysate.

25. Animal cells, which contain an isolated, purified gene according to claim 6 and the means necessary for its expression.

26. Animal cells, which contain an expression vector according to claim 12.

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End of Result Set

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L1: Entry 19 of 19 File: USPT Nov 16, 1971

US-PAT-NO: 3620923
DOCUMENT-IDENTIFIER: US 3620923 A

TITLE: URATE OXIDASE AND PROCESS FOR THE PRODUCTION THEREOF

DATE-ISSUED: November 16, 1971

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pierre Laboureur	Neuilly Seine	FR		
Marcel D. P. Brunaud	Paris	FR		
Claude Langlois	Montrouge	FR		

US-CL-CURRENT: 435/191; 435/815, 435/911, 435/912, 435/925, 435/931, 435/939

CLAIMS:

1. A process for producing a urate oxidase which promotes the oxidation of uric acid to allantoin which comprises cultivating under submerged aerobic conditions at a temperature of between 20.degree. and 35.degree. C. and at a pH in the range of 4 and 8, a micro-organism of a species of an order selected from the group consisting of eubacterialies, actiniomycetales, mucorales, moniliales, spheriales and endomycetales in an aqueous nutrient medium containing a source of assimilable carbon, a source of assimilable nitrogen and uric acid, to produce a micro-organism growth separating said growth, freezing the separated growth to below -10.degree. C., grinding the frozen growth, and extracting the ground growth with an aqueous medium containing a buffering

2. The process claimed in claim 1 in which the species is of a genus selected from the group consisting of Mucor, Rhizopus, Absidia, Fusarium, Alternaria, Penicillium, Aspergillus, Cephalosporium, Stemphylium,

3. The process claimed in claim 1 in which the resulting aqueous extract is treated with a water-soluble salt of a metal selected from calcium and

4. The process claimed in claim 3 in which the urate oxidase is precipitated from the resulting aqueous solution by the addition thereto of an organic liquid which is miscible with water and the precipitate

5. The process claimed in claim 3 in which the urate oxidase is precipitated from the resulting aqueous solution by the addition thereto

6. The process claimed in claim 4 in which the precipitated urate oxidase

7. The process claimed in claim 3 in which the precipitated urate oxidase is passed through a column of a cellulosic ion exchange material for

8. The process claimed in claim 3 in which the urate oxidase is passed through a column of material selected from dextran gel and polyacrylamide

9. The process claimed in claim 4 in which the precipitated urate oxidase is

further purified by reprecipitation from a solution in an aqueous

10. The process claimed in claim 4 in which the precipitated urate oxidase is further purified by absorption upon a substrate selected from hydroxyapatite, bentonite and alumina, subsequent extraction of the

11. The process claimed in claim 5 in which the precipitated urate oxidase

12. The process claimed in claim 5 in which the precipitated urate oxidase is further purified by reprecipitation from a solution in an aqueous

13. The process claimed in claim 5 in which the precipitated urate oxidase is further purified by absorption upon a substrate selected from hydroxyapatite, bentonite and alumina, subsequent extraction of the absorbate and elution with a saline solution.

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Search Results - Record(s) 21 through 24 of 24 returned.

☐ 21. Document ID: US 6015897 A

L3: Entry 21 of 24 File: USPT Jan 18, 2000

US-PAT-NO: 6015897
DOCUMENT-IDENTIFIER: US 6015897 A

TITLE: Biotinamido-n-methylglycyl-seryl-o-succinamido-benzyl dota

DATE-ISSUED: January 18, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Theodore; Louis J.	Lynnwood	WA		
Kasina; Sudhakar	Kirkland	WA		
Reno; John M.	Brier	WA		
Gustavson; Linda M.	Seattle	WA		

US-CL-CURRENT: 540/474

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 22. Document ID: US 5766897 A

L3: Entry 22 of 24 File: USPT Jun 16, 1998

US-PAT-NO: 5766897
DOCUMENT-IDENTIFIER: US 5766897 A
**** See image for Certificate of Correction ****

TITLE: Cysteine-pegylated proteins

DATE-ISSUED: June 16, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Braxton; Scott M.	San Mateo	CA		

US-CL-CURRENT: 435/463; 435/188, 435/212, 435/219

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 23. Document ID: US 5565519 A

L3: Entry 23 of 24 File: USPT Oct 15, 1996

US-PAT-NO: 5565519
DOCUMENT-IDENTIFIER: US 5565519 A

TITLE: Clear, chemically modified collagen-synthetic polymer conjugates for ophthalmic applications

DATE-ISSUED: October 15, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rhee; Woonza M.	Palo Alto	CA		
Rao; Prema R.	Los Gatos	CA		
Chu; George H.	Cupertino	CA		
DeLustro; Frank A.	Belmont	CA		

US-CL-CURRENT: 525/54.1; 523/113

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 24. Document ID: ZA 200207206 A WO 200159078 A2 AU 200149975 A BR 200108386 A EP 1254237 A2 CZ 200202982 A3 KR 2002087934 A HU 200204544 A2 JP 2003521937 W

L3: Entry 24 of 24 File: DWPI Jul 30, 2003

DERWENT-ACC-NO: 2001-570528
DERWENT-WEEK: 200355

TITLE: Purified urate oxidase substantially free of aggregates larger than octamers useful for treating elevated uric acid levels associated gout, tophi, renal insufficiency, organ transplantation and malignant disease

INVENTOR: SAIFER, M G P; SHERMAN, M R ; WILLIAMS, L D

PRIORITY-DATA: 2000US-0501730 (February 10, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
ZA 200207206 A	July 30, 2003		038	C12N000/00
WO 200159078 A2	August 16, 2001	E	023	C12N009/06
AU 200149975 A	August 20, 2001		000	C12N009/06
BR 200108386 A	October 29, 2002		000	C12N009/06
EP 1254237 A2	November 6, 2002	E	000	C12N015/53
CZ 200202982 A3	January 15, 2003		000	C12N009/06
KR 2002087934 A	November 23, 2002		000	C12N009/06
HU 200204544 A2	May 28, 2003		000	C12N015/53
JP 2003521937 W	July 22, 2003		036	C12N009/06

INT-CL (IPC): A61 K 38/44; A61 K 47/48; A61 P 19/06; C12 N 0/00; C12 N 9/06; C12 N 9/96; C12 N 15/53

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Terms	Documents
urate oxidase and aggregate	24

Display Format: - Change Format

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WEST Search History

DATE: Monday, September 08, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L3	urate oxidase and aggregate	24	L3
L2	urate oxidase and aggregate free	0	L2
L1	urate oxidase.clm.	19	L1

END OF SEARCH HISTORY

WEST

End of Result Set

Generate Collection Print

L1: Entry 1 of 1 File: USPT Jun 10, 2003

US-PAT-NO: 6576235
DOCUMENT-IDENTIFIER: US 6576235 B1

TITLE: PEG-urate oxidase conjugates and use thereof

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; L. David	Fremont	CA		
Hershfield; Michael S.	Durham	NC		
Kelly; Susan J.	Chapel Hill	NC		
Saifer; Mark G. P.	San Carlos	CA		
Sherman; Merry R.	San Carlos	CA		

US-CL-CURRENT: 424/94.4; 435/189, 435/191, 435/252.3, 435/320.1, 530/350, 536/23.2

CLAIMS:

What is claimed is:

1. A conjugate of uricase that retains at least about 75% of the uricolytic activity of unconjugated uricase and is substantially reduced in immunogenicity, comprising a purified uricase containing no more than about 10% non-tetrameric aggregated uricase, said purified uricase comprising subunits in which each subunit of the uricase is covalently linked to an average of 2 to 10 strands of PEG, wherein each molecule of PEG has a molecular weight between about 5.kDa and 100 kDa.

2. The conjugate of claim 1, wherein the uricase is mammalian uricase.

3. The conjugate of claim 2, wherein the uricase is porcine liver, bovine liver or ovine liver uricase.

4. The conjugate of claim 1, wherein the uricase is recombinant.

5. The conjugate of claim 4, wherein the uricase has the sequence of porcine, bovine, ovine or baboon liver uricase.

6. The conjugate of claim 4, wherein the uricase is chimeric.

7. The conjugate of claim 6, wherein the chimeric uricase contains portions of porcine liver and baboon liver uricase.

8. The conjugate of claim 7, wherein the chimeric uricase is pig-baboon chimeric uricase (PBC uricase).

9. The conjugate of claim 7, wherein the chimeric uricase is porcine uricase in which arginine residue 291 of SEQ ID NO:1 has been replaced by lysine (R291K) and threonine residue 301 of SEQ ID NO:1 has been replaced by serine (T301S) (PKS uricase).

10. The conjugate of claim 4, wherein the uricase has the sequence of baboon liver uricase (SEQ ID NO:2) in which tyrosine 97 has been replaced by histidine.

11. The conjugate of claim 4, wherein the uricase comprises an amino terminus and a carboxy terminus, and wherein the uricase is truncated at one terminus or both termini.

12. The conjugate of claim 1, wherein the uricase is a fungal or microbial uricase.

13. The conjugate of claim 12, wherein the fungal or microbial uricase is isolated from Apergillus flavus, Arthrobacter globiformis or Candida utilis, or is a recombinant enzyme having the sequence of one of those uricases.

14. The conjugate of claim 1, wherein the uricase is an invertebrate uricase.

15. The conjugate of claim 14, wherein the invertebrate uricase is isolated from Drosophila melanogaster or Drosophila pseudoobscura, or is a recombinant enzyme having the sequence of one of those uricases.

16. The conjugate of claim 1, wherein the uricase is a plant uricase.

17. The conjugate of claim 16, wherein the plant uricase is isolated from root nodules of Glycine max or is a recombinant enzyme having the sequence of that uricase.

18. The conjugate of claim 1, wherein the PEG has an average molecular weight between about 10 kDa and 60 kDa.

19. The conjugate of claim 18, wherein the PEG has an average molecular weight between about 20 kDa and 40 kDa.

20. The conjugate of claim 1, wherein the average number of covalently coupled strands of PEG is 3 to 8 strands per uricase subunit.

21. The conjugate of claim 20, wherein the average number of covalently coupled strands of PEG is 4 to 6 strands per uricase subunit.

22. The conjugate of claim 1, wherein the uricase is tetrameric.

23. The conjugate of claim 1, wherein the strands of PEG are covalently coupled to uricase via linkages selected from the group consisting of urethane linkages, secondary amine linkages, and amide linkages.

24. The conjugate of claim 1, wherein the PEG is linear.

25. The conjugate of claim 1, wherein the PEG is branched.

26. A pharmaceutical composition for lowering uric acid levels in a body fluid or tissue, comprising the conjugate of claim 1 and a pharmaceutically acceptable carrier.

27. The pharmaceutical composition of claim 26, wherein said composition is stabilized by lyophilization and dissolves promptly upon reconstitution to provide solutions suitable for parenteral administration.

28. The conjugate of claim 11, wherein said uricase is truncated at said amino terminus by deleting at least the first six amino acids from said amino terminus.

29. The conjugate of claim 11, wherein said uricase is truncated at said carboxyl terminus by deleting at least the last three amino acids from said carboxyl terminus.

30. The conjugate of claim 11, wherein said uricase is truncated at said amino

terminus and at said carboxyl terminus, by deleting at least the first six amino acids from said amino terminus and by deleting at least the last three amino acids from said carboxyl terminus.

31. The conjugate of claim 11, wherein said uricase is truncated at said amino terminus by deleting the first six amino acids from said amino terminus.

32. The conjugate of claim 11, wherein said uricase is truncated at said carboxyl terminus by deleting the last three amino acids from said carboxyl terminus.

33. The conjugate of claim 11, wherein said uricase is truncated at said amino terminus and at said carboxyl terminus, by deleting the first six amino acids from said amino terminus and by deleting the last three amino acids from said carboxyl terminus.

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End of Result Set

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L2: Entry 1 of 1 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166249
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030166249 A1

TITLE: PEG-urate oxidase conjugates and use thereof

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Williams, L. David	Fremont	CA	US	
Hershfield, Michael S.	Durham	NC	US	
Kelly, Susan J.	Chapel Hill	NC	US	
Saifer, Mark G. P.	San Carlos	CA	US	
Sherman, Merry R.	San Carlos	CA	US	

APPL-NO: 09/ 839946 [PALM]
DATE FILED: April 19, 2001

RELATED-US-APPL-DATA:
Application 09/839946 is a division-of US application 09/370084, filed August 6, 1999, US Patent No. 6576235

INT-CL: [07] C12 N 9/78, C12 P 21/02, C12 N 5/06, C12 N 1/21, C12 N 1/16, C12 N 1/18

US-CL-PUBLISHED: 435/227; 435/69.1, 435/252.3, 435/254.2, 435/325, 435/320.1
US-CL-CURRENT: 435/227; 435/252.3, 435/254.2, 435/320.1, 435/325, 435/69.1

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

A naturally occurring or recombinant urate oxidase (uricase) covalently coupled to poly(ethylene glycol) or poly(ethylene oxide) (both referred to as PEG), wherein an average of 2 to 10 strands of PEG are conjugated to each uricase subunit and the PEG has an average molecular weight between about 5 kDa and 100 kDa. The resulting PEG-uricase conjugates are substantially non-immunogenic and retain at least 75% of the uricolytic activity of the unmodified enzyme.

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Search Results - Record(s) 1 through 7 of 7 returned.

☐ 1. Document ID: US 20030166249 A1

L7: Entry 1 of 7 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166249
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030166249 A1

TITLE: PEG-urate oxidase conjugates and use thereof

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Williams, L. David	Fremont	CA	US	
Hershfield, Michael S.	Durham	NC	US	
Kelly, Susan J.	Chapel Hill	NC	US	
Saifer, Mark G. P.	San Carlos	CA	US	
Sherman, Merry R.	San Carlos	CA	US	

US-CL-CURRENT: 435/227; 435/252.3, 435/254.2, 435/320.1, 435/325, 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 2. Document ID: US 20020090738 A1

L7: Entry 2 of 7 File: PGPB Jul 11, 2002

PGPUB-DOCUMENT-NUMBER: 20020090738
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020090738 A1

TITLE: System and method of microdispensing and arrays of biolayers provided by same

PUBLICATION-DATE: July 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cozzette, Stephen N.	Nepean	NJ	CA	
Davis, Graham	Plainsboro	PA	US	
Lauks, Imants R.	Yardley	PA	US	
Mier, Randall M.	Morrisville	NJ	US	
Piznik, Sylvia	Jackson	NJ	US	
Smit, Nicolaas	Hightstown	NJ	US	
Van Der Werf, Paul	Princeton Junction	NJ	US	
Wieck, Henry J.	Plainsboro		US	

US-CL-CURRENT: 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 3. Document ID: US 6576235 B1

L7: Entry 3 of 7 File: USPT Jun 10, 2003

US-PAT-NO: 6576235
DOCUMENT-IDENTIFIER: US 6576235 B1

TITLE: PEG-urate oxidase conjugates and use thereof

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; L. David	Fremont	CA		
Hershfield; Michael S.	Durham	NC		
Kelly; Susan J.	Chapel Hill	NC		
Saifer; Mark G. P.	San Carlos	CA		
Sherman; Merry R.	San Carlos	CA		

US-CL-CURRENT: 424/94.4; 435/189, 435/191, 435/252.3, 435/320.1, 530/350, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc | Image

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☐ 4. Document ID: US 6306594 B1

L7: Entry 4 of 7 File: USPT Oct 23, 2001

US-PAT-NO: 6306594
DOCUMENT-IDENTIFIER: US 6306594 B1

TITLE: Methods for microdispensing patterened layers

DATE-ISSUED: October 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cozzette; Stephen N.	Nepean			CA
Davis; Graham	Plainsboro	NJ		
Lauks; Imants R.	Yardley	PA		
Mier; Randall M.	Morrisvile	PA		
Piznik; Sylvia	Jackson	NJ		
Smit; Nicolaas	Hightstown	NJ		
Van der Werf; Paul	Princeton Junction	NJ		
Wieck; Henry J.	Plainsboro	NJ		

US-CL-CURRENT: 435/6; 430/127, 430/14, 430/16, 430/4, 430/5, 430/56, 430/96, 430/97, 435/174, 435/180, 435/4, 435/5, 436/518, 436/524, 436/525, 436/531

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 5. Document ID: US 5554339 A

L7: Entry 5 of 7 File: USPT Sep 10, 1996

US-PAT-NO: 5554339
DOCUMENT-IDENTIFIER: US 5554339 A
**** See image for Certificate of Correction ****

TITLE: Process for the manufacture of wholly microfabricated biosensors

DATE-ISSUED: September 10, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cozzette; Stephen N.	Nepean			CA
Davis; Graham	Plainsboro	NJ		
Lauks; Imants R.	Yardley	PA		
Mier; Randall M.	Morrisvile	PA		
Piznik; Sylvia	Jackson	NJ		
Smit; Nicolaas	Hightstown	NJ		
Van Der Werf; Paul	Princeton Junction	NJ		
Wieck; Henry J.	Plainsboro	NJ		

US-CL-CURRENT: 422/50; 422/63, 422/68.1, 422/69, 422/78, 422/79, 422/82.05, 435/6, 436/501

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 6. Document ID: US 5466575 A

L7: Entry 6 of 7 File: USPT Nov 14, 1995

US-PAT-NO: 5466575
DOCUMENT-IDENTIFIER: US 5466575 A

TITLE: Process for the manufacture of wholly microfabricated biosensors

DATE-ISSUED: November 14, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cozzette; Stephen N.	Nepean			CA
Davis; Graham	Plainsboro	NJ		
Lauks; Imants R.	Yardley	PA		
Mier; Randall M.	Morrisvile	PA		
Piznik; Sylvia	Jackson	NJ		
Smit; Nicolaas	Hightstown	NJ		
Van Der Werf; Paul	Princeton Junction	NJ		
Wieck; Henry J.	Plainsboro	NJ		

US-CL-CURRENT: 435/6; 204/403.1, 204/403.11, 204/403.12, 204/411, 204/412, 204/414, 204/415, 204/416, 204/417, 204/418, 204/419, 204/430, 204/431, 204/432, 422/82.01, 427/2.13, 427/96, 430/315, 435/177, 435/817, 436/149, 436/806, 438/1, 438/107, 438/110, 438/49, 438/67

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw. Desc

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☐ 7. Document ID: US 5200051 A

L7: Entry 7 of 7 File: USPT Apr 6, 1993

US-PAT-NO: 5200051
DOCUMENT-IDENTIFIER: US 5200051 A

TITLE: Wholly microfabricated biosensors and process for the manufacture and use thereof

DATE-ISSUED: April 6, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cozzette; Stephen N.	Nepean			CA
Davis; Graham	Plainsboro	NJ		
Itak; Jeanne A.	North Brunswick	NJ		
Lauks; Imants R.	Yardley	PA		
Mier; Randall M.	Morrisville	PA		
Piznik; Sylvia	Jackson	NJ		
Smit; Nicolaas	Hightstown	NJ		
Steiner; Susan J.	Trenton	NJ		
Van Der Werf; Paul	Princeton Junction	NJ		
Wieck; Henry J.	Plainsboro	NJ		

US-CL-CURRENT: 204/403.07; 204/403.09, 204/403.1, 204/403.11, 204/403.13, 204/415, 205/778, 205/782.5, 257/253, 422/930 , 435/287.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw. Desc

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15 and subunit?	7

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Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 20030166249 A1

L8: Entry 1 of 3 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166249
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030166249 A1

TITLE: PEG-urate oxidase conjugates and use thereof

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Williams, L. David	Fremont	CA	US	
Hershfield, Michael S.	Durham	NC	US	
Kelly, Susan J.	Chapel Hill	NC	US	
Saifer, Mark G. P.	San Carlos	CA	US	
Sherman, Merry R.	San Carlos	CA	US	

US-CL-CURRENT: 435/227; 435/252.3, 435/254.2, 435/320.1, 435/325, 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6576235 B1

L8: Entry 2 of 3 File: USPT Jun 10, 2003

US-PAT-NO: 6576235
DOCUMENT-IDENTIFIER: US 6576235 B1

TITLE: PEG-urate oxidase conjugates and use thereof

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; L. David	Fremont	CA		
Hershfield; Michael S.	Durham	NC		
Kelly; Susan J.	Chapel Hill	NC		
Saifer; Mark G. P.	San Carlos	CA		
Sherman; Merry R.	San Carlos	CA		

US-CL-CURRENT: 424/94.4; 435/189, 435/191, 435/252.3, 435/320.1, 530/350, 536/23.2

☐ 3. Document ID: NZ 509633 A WO 200008196 A2 AU 9953365 A EP 1100880 A2 BR 9913360 A CZ 200100466 A3 KR 2001053633 A HU 200103205 A2 CN 1322243 A ZA 200100974 A JP 2002524053 W MX 2001001342 A1

L8: Entry 3 of 3 File: DWPI Apr 29, 2003

DERWENT-ACC-NO: 2000-195586
DERWENT-WEEK: 200334

TITLE: Recombinant mammalian uricase protein which used to treat elevated uric acid levels associated with e.g. gout is modified by the insertion of one or more lysine residues

INVENTOR: HERSHFIELD, M; KELLY, S J

PRIORITY-DATA: 1998US-095489P (August 6, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NZ 509633 A	April 29, 2003		000	C12N015/12
WO 200008196 A2	February 17, 2000	E	069	C12N009/09
AU 9953365 A	February 28, 2000		000	C12N015/00
EP 1100880 A2	May 23, 2001	E	000	C12N009/00
BR 9913360 A	July 3, 2001		000	C12N009/00
CZ 200100466 A3	July 11, 2001		000	C12N009/06
KR 2001053633 A	June 25, 2001		000	C12N009/06
HU 200103205 A2	December 28, 2001		000	C12N015/00
CN 1322243 A	November 14, 2001		000	C12N009/00
ZA 200100974 A	June 26, 2002		083	A61K000/00
JP 2002524053 W	August 6, 2002		075	C12N015/09
MX 2001001342 A1	October 1, 2001		000	A61K038/54

INT-CL (IPC): A61 K 0/00; A61 K 38/44; A61 K 38/54; A61 K 48/00; A61 P 19/06; C07 H 21/04; C12 N 1/15; C12 N 1/19; C12 N 1/21; C12 N 5/10; C12 N 9/00; C12 N 9/02; C12 N 9/06; C12 N 9/09; C12 N 15/00; C12 N 15/09; C12 N 15/12; C12 N 15/52; C12 N 15/63

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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Terms	Documents
baboon uricase	3

Display Format: - Change Format

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WEST

End of Result Set

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L9: Entry 1 of 1 File: DWPI Apr 29, 2003

DERWENT-ACC-NO: 2000-195586
DERWENT-WEEK: 200334

TITLE: Recombinant mammalian uricase protein which used to treat elevated uric acid levels associated with e.g. gout is modified by the insertion of one or more lysine residues

INVENTOR: HERSHFIELD, M; KELLY, S J

PRIORITY-DATA: 1998US-095489P (August 6, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NZ 509633 A	April 29, 2003		000	C12N015/12
WO 200008196 A2	February 17, 2000	E	069	C12N009/09
AU 9953365 A	February 28, 2000		000	C12N015/00
EP 1100880 A2	May 23, 2001	E	000	C12N009/00
BR 9913360 A	July 3, 2001		000	C12N009/00
CZ 200100466 A3	July 11, 2001		000	C12N009/06
KR 2001053633 A	June 25, 2001		000	C12N009/06
HU 200103205 A2	December 28, 2001		000	C12N015/00
CN 1322243 A	November 14, 2001		000	C12N009/00
ZA 200100974 A	June 26, 2002		083	A61K000/00
JP 2002524053 W	August 6, 2002		075	C12N015/09
MX 2001001342 A1	October 1, 2001		000	A61K038/54

INT-CL (IPC): A61 K 0/00; A61 K 38/44; A61 K 38/54; A61 K 48/00; A61 P 19/06; C07 H 21/04; C12 N 1/15; C12 N 1/19; C12 N 1/21; C12 N 5/10; C12 N 9/00; C12 N 9/02; C12 N 9/06; C12 N 9/09; C12 N 15/00; C12 N 15/09; C12 N 15/12; C12 N 15/52; C12 N 15/63

ABSTRACTED-PUB-NO: WO 200008196A
BASIC-ABSTRACT:

NOVELTY - Chimeric recombinant mammalian urate oxidase (uricase) protein (I) having one or more lysine residues inserted, is new.

DETAILED DESCRIPTION - (I) comprises a defined sequence of either;

(a) 304 amino acids (aa) where the N-terminal 225 aa correspond to aa 1-225 of porcine uricase and the C-terminal 79 aa correspond to aa 226-304 of baboon uricase;

(b) 304 amino acids (aa) where the N-terminal 288 aa correspond to aa 1-288 of porcine uricase and the C-terminal 16 aa correspond to aa 289-304 of baboon uricase; or

(c) 304, 304, 298, 301, 298, or 301 aa,

(all given in the specification).

INDEPENDENT CLAIMS are also included for:

(1) polynucleotides encoding (I) having a defined sequence of 915 or 915 bp (given in the specification);

(2) vectors comprising a polynucleotide as in (1); and

(3) host cells comprising the vector as in (2).

ACTIVITY - Antigout; cytostatic.

MECHANISM OF ACTION - In mammals uricase converts urate to allantonin (+CO2 and H2O2) which is 80-100 times more soluble than uric acid and can be handled more efficiently by the kidneys.

USE - The proteins are modified to increase the available non-deleterious monomethoxypolyethylene glycol (PEG) attachment sites (claimed) and so enhance the ability of PEG to mask potentially immunogenic epitopes when attached. The proteins can thus be used to produce improved PEG-uricase conjugates with reduced immunogenicity and also improved bioavailability (e.g. through improved solubility and biological half-life), useful for lowering the levels of uric acid in the blood and/or urine of mammals (especially humans) e.g. to treat elevated uric acid levels associated with gout, tophi, renal insufficiency, organ transplantation or malignant disease. Such conjugates can be included in pharmaceutical compositions useful to treat conditions as above, e.g. to decrease the need for hemodialysis in patients with a high risk of urate-induced kidney failure such as organ transplant patients.

ADVANTAGE - PEG attachment (PEGylation) has previously been shown to reduce the immunogenicity and prolong the circulating life of fungal and porcine uricases in animals, and the modified proteins enhance the ability of PEG to mask potentially immunogenic epitopes compared to unmodified uricases. The preferred chimeric proteins may also have reduced immunoreactivity in humans, since they are derived from mammalian rather than more distantly related fungal or bacterial sequences; proteins PBC and PKS are especially advantageous since they comprise pig and baboon sequences which are highly homologous to the published human sequence. For example, intraperitoneal injections of PEGylated PBC to a uricase-deficient knock-out mouse having high uric acid levels in its blood and bodily fluid (0 and 72 h; 0.4 International Units (IU; one IU=amount of enzyme consuming 1 micro M uric acid/min.)) resulted in increased serum uricase activity and a marked decline in serum and urinary uric acid concentrations.

ABSTRACTED-PUB-NO: WO 200008196A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/14

WEST

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Search Results - Record(s) 11 through 20 of 46 returned.

☐ 11. Document ID: US 6576235 B1

L5: Entry 11 of 46 File: USPT Jun 10, 2003

US-PAT-NO: 6576235
DOCUMENT-IDENTIFIER: US 6576235 B1

TITLE: PEG-urate oxidase conjugates and use thereof

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; L. David	Fremont	CA		
Hershfield; Michael S.	Durham	NC		
Kelly; Susan J.	Chapel Hill	NC		
Saifer; Mark G. P.	San Carlos	CA		
Sherman; Merry R.	San Carlos	CA		

US-CL-CURRENT: 424/94.4; 435/189, 435/191, 435/252.3, 435/320.1, 530/350, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 12. Document ID: US 6455261 B1

L5: Entry 12 of 46 File: USPT Sep 24, 2002

US-PAT-NO: 6455261
DOCUMENT-IDENTIFIER: US 6455261 B1

TITLE: Diagnostic assay using microperoxidase

DATE-ISSUED: September 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wong; Sie-Ting	Mundelein	IL	60060	
Lee; Sung-Chul	Libertyville	IL	60048	

US-CL-CURRENT: 435/7.1; 435/10, 435/7.9, 435/7.91

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 13. Document ID: US 6395299 B1

L5: Entry 13 of 46 File: USPT May 28, 2002

US-PAT-NO: 6395299
DOCUMENT-IDENTIFIER: US 6395299 B1

TITLE: Matrices for drug delivery and methods for making and using the same

DATE-ISSUED: May 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Babich; John W.	Scituate	MA		
Zubieta; Jon	Syracuse	NY		
Bonavia; Grant	Kensington	MD		

US-CL-CURRENT: 424/484

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 14. Document ID: US 6306594 B1

L5: Entry 14 of 46 File: USPT Oct 23, 2001

US-PAT-NO: 6306594
DOCUMENT-IDENTIFIER: US 6306594 B1

TITLE: Methods for microdispensing patterened layers

DATE-ISSUED: October 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cozzette; Stephen N.	Nepean			CA
Davis; Graham	Plainsboro	NJ		
Lauks; Imants R.	Yardley	PA		
Mier; Randall M.	Morrisvile	PA		
Piznik; Sylvia	Jackson	NJ		
Smit; Nicolaas	Hightstown	NJ		
Van der Werf; Paul	Princeton Junction	NJ		
Wieck; Henry J.	Plainsboro	NJ		

US-CL-CURRENT: 435/6; 430/127, 430/14, 430/16, 430/4, 430/5, 430/56, 430/96, 430/97, 435/174, 435/180, 435/4, 435/5, 436/518, 436/524, 436/525, 436/531

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 15. Document ID: US 6159699 A

L5: Entry 15 of 46 File: USPT Dec 12, 2000

US-PAT-NO: 6159699
DOCUMENT-IDENTIFIER: US 6159699 A

TITLE: Enzyme linked chemiluminescent assay

DATE-ISSUED: December 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; Richard Charles	Cardiff			GB
Weeks; Ian	Cardiff			GB

US-CL-CURRENT: 435/7.1; 435/6, 435/7.5, 435/7.9, 435/7.91, 435/7.92, 435/966, 435/968, 435/975, 436/501

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 16. Document ID: US 5880255 A

L5: Entry 16 of 46 File: USPT Mar 9, 1999

US-PAT-NO: 5880255
DOCUMENT-IDENTIFIER: US 5880255 A
**** See image for Certificate of Correction ****

TITLE: Process for fractionating polyethylene glycol (PEG)-protein adducts and an adduct of PEG and granulocyte-macrophage colony stimulating factor

DATE-ISSUED: March 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Delgado; Cristina	London			GB
Francis; Gillian Elizabeth	London			GB
Fisher; Derek	London			GB

US-CL-CURRENT: 530/303; 424/179.1, 424/85.1, 424/94.3, 435/188, 530/345, 530/351, 530/391.9, 530/408, 530/410

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 17. Document ID: US 5637749 A

L5: Entry 17 of 46 File: USPT Jun 10, 1997

US-PAT-NO: 5637749
DOCUMENT-IDENTIFIER: US 5637749 A

TITLE: Aryl imidate activated polyalkylene oxides

DATE-ISSUED: June 10, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		

US-CL-CURRENT: 558/6; 530/385, 604/20

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 18. Document ID: US 5631322 A

L5: Entry 18 of 46 File: USPT May 20, 1997

US-PAT-NO: 5631322
DOCUMENT-IDENTIFIER: US 5631322 A
**** See image for Certificate of Correction ****

TITLE: Polymers of N-acryloylmorpholine activated at one end and conjugates with bioactive materials and surfaces

DATE-ISSUED: May 20, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Veronese; Francesco M.	Padua			IT
Schiavon; Oddone	Padua			IT
Caliceti; Paolo	Padua			IT
Sartore; Luciana	Marano Vic.			IT
Ranucci; Elisabetta	Brescia			IT
Ferruti; Paolo	Milan			IT

US-CL-CURRENT: 525/54.1; 525/326.1, 525/326.8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 19. Document ID: US 5567422 A

L5: Entry 19 of 46 File: USPT Oct 22, 1996

US-PAT-NO: 5567422
DOCUMENT-IDENTIFIER: US 5567422 A

TITLE: Azlactone activated polyalkylene oxides conjugated to biologically active nucleophiles

DATE-ISSUED: October 22, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		

US-CL-CURRENT: 424/78.3; 424/78.38, 525/54.1, 530/815

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 20. Document ID: US 5559003 A

L5: Entry 20 of 46 File: USPT Sep 24, 1996

US-PAT-NO: 5559003
DOCUMENT-IDENTIFIER: US 5559003 A

TITLE: Assay method for biological components

DATE-ISSUED: September 24, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kawahara; Sumi	Tokyo			JP
Abe; Toshikatsu	Tokyo			JP
Hosoi; Kenji	Tokyo			JP

US-CL-CURRENT: 435/28; 435/10, 435/11, 435/12, 435/14, 435/17, 435/18, 435/21, 435/25, 435/4, 436/12, 436/13, 436/14, 436/63, 436/71, 436/74

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Terms	Documents
bovine and uricase.clm.	46

Display Format: - Change Format

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WEST Search History

DATE: Monday, September 08, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L12	plant uricase.clm.	2	L12
L11	microbial uricase.clm.	2	L11
L10	mammalian uricase.clm.	2	L10
L9	Recombinant mammalian uricase	1	L9
L8	baboon uricase	3	L8
L7	l5 and subunit?	7	L7
L6	l5 and tetramer	2	L6
L5	bovine and uricase.clm.	46	L5
L4	porcine and uricase.clm.	6	L4
L3	tetrameric and uricase.clm.	2	L3
L2	tetrameric uricase.clm.	1	L2
DB=USPT; PLUR=YES; OP=ADJ			
L1	6576235	1	L1

END OF SEARCH HISTORY

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FULL ESTIMATED COST                                         0.21       0.21

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=> s purified uricase and free of aggregates
L1            1 PURIFIED URICASE AND FREE OF AGGREGATES

=> d l1 ibib ab

L1    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-00996  BIOTECHDS
TITLE:            Purified urate-oxidase substantially free of
                  aggregates larger than octamers useful for treating
                  elevated uric acid levels associated gout, tophi, renal
                  insufficiency, organ transplantation and malignant disease;
                     human, pig liver, fungus, plant recombinant uricase useful
                     in disease therapy
AUTHOR:           Sherman M R; Saifer M G P; Williams L D
PATENT ASSIGNEE:  Mountain-View-Pharmaceuticals
LOCATION:         Menlo Park, CA, USA.
PATENT INFO:      WO 2001059078 16 Aug 2001
APPLICATION INFO: WO 2001-US40069 7 Feb 2001
PRIORITY INFO:    US 2000-501730 10 Feb 2000
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2001-570528 [64]
AB    A purified urate-oxidase (uricase (EC-1.7.3.3)) (I) substantially
      free of aggregates larger than octamers, is claimed.
      (I) is a mammalian uricase, or pig liver, cattle liver, ovine liver or
      baboon liver uricase, fungal uricase, microbial uricase or plant uricase.
      (I) is a recombinant or chimeric uricase.  Also claimed are: a
      pharmaceutical composition (II) for lowering uric acid levels in the body
      fluid or tissue; purification (M) of (I) having reduced immunogenicity,
      involves separating uricase aggregates larger than octamers in uricase
      fractions, where the separation is performed by ionexchange
      chromatography, size-exclusion chromatography or ultrafiltration, and
      excluding the aggregates from the purified uricase;
      and an isolated uricase (III) prepared by (M).  (II) is useful for
      lowering the levels of uric acid in a body fluid or tissue of humans and
      for treating elevated uric acid levels associated with conditions
      including gout, tophi, renal insufficiency, organ transplantation and
      malignant disease.  (23pp)


=> s purified uricase
```

L2 57 PURIFIED URICASE

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 41 DUP REM L2 (16 DUPLICATES REMOVED)

=> s l3 and mammal?
L4 3 L3 AND MAMMAL?

=> d l4 1-3 ibib ab

L4 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 87160694 MEDLINE
DOCUMENT NUMBER: 87160694 PubMed ID: 3493879
TITLE: Comparison of intraperoxisomal localization form and properties of amphibian (Rana catesbeiana) uricase with those of other animal uricases.
AUTHOR: Fujiwara S; Ohashi H; Noguchi T
SOURCE: COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY. B: COMPARATIVE BIOCHEMISTRY, (1987) 86 (1) 23-6.
Journal code: 2984730R. ISSN: 0305-0491.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198704
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19900303
Entered Medline: 19870427

AB Liver uricase of bull frog (Rana catesbeiana) was present as the soluble form in the peroxisomal matrix and consisted of four identical subunits with a molecular weight of 30,000. These properties were identical with those of fish liver uricase but differed from **mammalian** liver uricase. **Purified uricase** from the frog liver was insoluble in hypertonic, hypotonic and detergent solutions at pH 6-9. This insolubility was the same as **mammalian** liver uricase but differed from fish liver uricase; fish uricase was soluble in these solutions. The frog liver uricase did not cross-react immunologically with both uricases of fish and **mammalian** liver. An immunological cross-reactivity of liver uricase was observed among amphibia.

L4 ANSWER 2 OF 3 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-00996 BIOTECHDS
TITLE: Purified urate-oxidase substantially free of aggregates larger than octamers useful for treating elevated uric acid levels associated gout, tophi, renal insufficiency, organ transplantation and malignant disease;
human, pig liver, fungus, plant recombinant uricase useful in disease therapy
AUTHOR: Sherman M R; Saifer M G P; Williams L D
PATENT ASSIGNEE: Mountain-View-Pharmaceuticals
LOCATION: Menlo Park, CA, USA.
PATENT INFO: WO 2001059078 16 Aug 2001
APPLICATION INFO: WO 2001-US40069 7 Feb 2001
PRIORITY INFO: US 2000-501730 10 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-570528 [64]

AB A purified urate-oxidase (uricase (EC-1.7.3.3)) (I) substantially free of aggregates larger than octamers, is claimed. (I) is a **mammalian** uricase, or pig liver, cattle liver, ovine liver or baboon liver uricase, fungal uricase, microbial uricase or plant uricase. (I) is a recombinant or chimeric uricase. Also claimed are: a pharmaceutical composition (II) for lowering uric acid levels in the body fluid or tissue; purification

(M) of (I) having reduced immunogenicity, involves separating uricase aggregates larger than octamers in uricase fractions, where the separation is performed by ionexchange chromatography, size-exclusion chromatography or ultrafiltration, and excluding the aggregates from the **purified uricase**; and an isolated uricase (III) prepared by (M). (II) is useful for lowering the levels of uric acid in a body fluid or tissue of humans and for treating elevated uric acid levels associated with conditions including gout, tophi, renal insufficiency, organ transplantation and malignant disease. (23pp)

L4 ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-07139 BIOTECHDS
TITLE: New non-immunogenic conjugates useful for treating arthritis, tophi and renal failure associated with gout, comprises polyethylene glycol and uricase that retains 75% of the uricolytic activity of unconjugated uricase;
uricase chimeric enzyme, produced by enzyme engineering, used to treat gout, tophi and kidney failure
AUTHOR: Williams L D; Hershfield M S; Kelly S J; Saifer M G P; Sherman M R
PATENT ASSIGNEE: Mountainview-Pharmaceuticals; Univ.Duke
LOCATION: Menlo Park, CA, USA; Durham, NC, USA.
PATENT INFO: WO 2000007629 17 Feb 2000
APPLICATION INFO: WO 1999-US17514 2 Aug 1999
PRIORITY INFO: US 1998-130392 6 Aug 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-237330 [20]
AB A substantially non-immunogenic uricase (EC-1.7.3.3) conjugate (I), that retains 75% of the uricolytic activity of unconjugated uricase, is claimed. (I) consists of **purified uricase** subunits covalently linked to 2-10 strands of polyethylene glycol with mol.wt. of 5,000-100,000 each. Also claimed is a means of isolating a tetrameric form of uricase, and a tetrameric uricase isolated by that technique. (I) can be used to lower elevated uric acid levels in body fluids or tissues of a **mammal**. This can be used to treat gout, tophi, kidney deficiency, immune response associated with organ transplantation, or malignant disease. (I) reduces the need for hemodialysis. It specifically contains a pig-baboon uricase fusion protein, or a pig-mutant pig uricase fusion protein, in which Arg291 is substituted with Lys, and Thr301 is substituted with Ser. The pig and baboon uricase enzymes have given 304 amino acid protein sequences. The PEG preferably consists of 4-6 strands of linear, especially monomethoxy PEG or branched PEG, with a mol.wt. of 20-40,000. (52pp)

=> s l3 and (porcine or bovine or ovine liver or baboon)
L5 5 L3 AND (PORCINE OR BOVINE OR OVINE LIVER OR BABOON)

=> d l5 ibib ab

L5 ANSWER 1 OF 5 MEDLINE on STN
ACCESSION NUMBER: 77193853 MEDLINE
DOCUMENT NUMBER: 77193853 PubMed ID: 559302
TITLE: Purification of uricase by biospecific adsorption-desorption.
AUTHOR: Batista-Viera F; Axen R; Carlsson J
SOURCE: PREPARATIVE BIOCHEMISTRY, (1977) 7 (2) 103-10.
Journal code: 1276634. ISSN: 0032-7484.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197707
ENTRY DATE: Entered STN: 19900314

Last Updated on STN: 19900314
Entered Medline: 19770729

AB A simple procedure for the purification of uricase from **bovine** kidney is described. The procedure involves the following steps: 1) processing of kidney mince by borate/butanol, 2) ammonium sulphate precipitation, and 3) biospecific adsorption-desorption. The adsorbents were prepared by chemical attachment of urate or xanthine to agarose gel beads. The desorption was performed by a xanthine solution. The adsorption-desorption procedure resulted in an 11 000-12 000-fold purification. The specific activity of the **purified uricase** was 19.8 U/mg using either "urate" adsorbent. The recovery was about 70%. The adsorbents were also used for the purification of commercial uricase preparations from hog liver. In this case the **purified uricase** also possessed a specific activity of 19.8 U/mg. The products were homogenous as judged by gradipore electrophoresis and gel filtration.

=> s l3 and (fly or plant or fungus or bacteria)
L6 1 L3 AND (FLY OR PLANT OR FUNGUS OR BACTERIA)

=> d 16 ibib ab

L6 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-00996 BIOTECHDS
TITLE: Purified urate-oxidase substantially free of aggregates larger than octamers useful for treating elevated uric acid levels associated gout, tophi, renal insufficiency, organ transplantation and malignant disease;
human, pig liver, **fungus**, **plant** recombinant uricase useful in disease therapy
AUTHOR: Sherman M R; Saifer M G P; Williams L D
PATENT ASSIGNEE: Mountain-View-Pharmaceuticals
LOCATION: Menlo Park, CA, USA.
PATENT INFO: WO 2001059078 16 Aug 2001
APPLICATION INFO: WO 2001-US40069 7 Feb 2001
PRIORITY INFO: US 2000-501730 10 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-570528 [64]
AB A purified urate-oxidase (uricase (EC-1.7.3.3)) (I) substantially free of aggregates larger than octamers, is claimed. (I) is a mammalian uricase, or pig liver, cattle liver, ovine liver or baboon liver uricase, fungal uricase, microbial uricase or **plant** uricase. (I) is a recombinant or chimeric uricase. Also claimed are: a pharmaceutical composition (II) for lowering uric acid levels in the body fluid or tissue; purification (M) of (I) having reduced immunogenicity, involves separating uricase aggregates larger than octamers in uricase fractions, where the separation is performed by ionexchange chromatography, size-exclusion chromatography or ultrafiltration, and excluding the aggregates from the **purified uricase**; and an isolated uricase (III) prepared by (M). (II) is useful for lowering the levels of uric acid in a body fluid or tissue of humans and for treating elevated uric acid levels associated with conditions including gout, tophi, renal insufficiency, organ transplantation and malignant disease. (23pp)

=> s (uricase or urate oxidase) and dna
L7 340 (URICASE OR URATE OXIDASE) AND DNA

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 194 DUP REM L7 (146 DUPLICATES REMOVED)

=> s l8 and (rat or mice or babbon or porcine or pig or ovine or bovine)

L9 72 L8 AND (RAT OR MICE OR BABBON OR PORCINE OR PIG OR OVINE OR BOVINE)

=> s l9 and aggregate?
L10 1 L9 AND AGGREGATE?

=> d l10

L10 ANSWER 1 OF 1 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 92177764 EMBASE
DN 1992177764
TI **Rat urate oxidase** produced by recombinant baculovirus expression: Formation of peroxisome crystalloid core-like structures.
AU Alvares K.; Widrow R.J.; Abu-Jawdeh G.M.; Schmidt J.V.; Yeldandi A.V.; Rao M.S.; Reddy J.K.
CS Department of Pathology, Northwestern University Med. School, 303 East Chicago Avenue,Chicago, IL 60611, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1992) 89/11 (4908-4912).
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English

=> d l10 ab

L10 ANSWER 1 OF 1 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AB **Urate oxidase** (EC 1.7.3.3), which catalyzes the oxidation of uric acid to allantoin, is present in most mammals but absent in humans and hominoid primates. In rats and most other mammals that catabolize uric acid to allantoin, this enzyme is localized within the crystalloid cores of peroxisomes present in liver parenchymal cells. To determine whether **urate oxidase** forms these crystalloid cores or whether core-forming protein(s) exist in association with **urate oxidase**, a baculovirus expression vector system was used to overproduce the full-length **rat urate oxidase** in Spodoptera frugiperda cells. **Urate oxidase** was expressed to a level of .simeq.30% of the total protein in this system. Immunoblot analysis demonstrated that the baculovirus-generated protein had electrophoretic and immunologic properties similar to those of **urate oxidase** expressed in **rat** liver. Immunofluorescence and electron microscopic examination revealed that the overexpressed recombinant **urate oxidase** is present in both the cytoplasm and the nucleus of infected insect cells as numerous 1- to 3-.mu.m discrete particles. These insoluble protein **aggregates**, which were positively stained for **urate oxidase** by protein A-gold immunocytochemical approach, did not appear to be delimited by a single membrane. They revealed a crystalloid structure reminiscent of **rat** peroxisomal core consisting of bundles of tubules with an inner diameter of .simeq.50 .ANG.. The recombinant **urate oxidase** particles, isolated by a single-step procedure, were composed entirely of 35- kDa **urate oxidase** subunit. These studies indicate that **rat urate oxidase** is capable of forming insoluble crystalloid core-like structures.

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

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FULL ESTIMATED COST                                    78.93      79.14

FILE 'STNGUIDE' ENTERED AT 11:35:09 ON 08 SEP 2003
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep  5, 2003 (20030905/UP).

=> d his

     (FILE 'HOME' ENTERED AT 11:23:59 ON 08 SEP 2003)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOTECHDS, SCISEARCH, BIOSIS' ENTERED AT
     11:24:34 ON 08 SEP 2003
L1             1 S PURIFIED URICASE AND FREE OF AGGREGATES
L2            57 S PURIFIED URICASE
L3            41 DUP REM L2 (16 DUPLICATES REMOVED)
L4             3 S L3 AND MAMMAL?
L5             5 S L3 AND (PORCINE OR BOVINE OR OVINE LIVER  OR BABOON)
L6             1 S L3 AND (FLY OR PLANT OR FUNGUS OR BACTERIA)
L7           340 S (URICASE OR URATE OXIDASE) AND DNA
L8           194 DUP REM L7 (146 DUPLICATES REMOVED)
L9            72 S L8 AND (RAT OR MICE OR BABBON OR PORCINE OR PIG OR OVINE OR
L10            1 S L9 AND AGGREGATE?

     FILE 'STNGUIDE' ENTERED AT 11:35:09 ON 08 SEP 2003

=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.36      79.50

STN INTERNATIONAL LOGOFF AT 11:38:40 ON 08 SEP 2003
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=> file medline caplus embase biosis biotechds
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:12:27 ON 10 SEP 2003

FILE 'CAPLUS' ENTERED AT 11:12:27 ON 10 SEP 2003
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FILE 'EMBASE' ENTERED AT 11:12:27 ON 10 SEP 2003
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FILE 'BIOSIS' ENTERED AT 11:12:27 ON 10 SEP 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'BIOTECHDS' ENTERED AT 11:12:27 ON 10 SEP 2003
COPYRIGHT (C) 2003 THOMSON DERWENT AND INSTITUTE FOR SCIENTIFIC INFORMATION

=> s porcine uricase and (291 or 301 or 97)
L1            0 PORCINE URICASE AND (291 OR 301 OR 97)

=> s porcine and uricase and (291 or 301 or 97)
L2            1 PORCINE AND URICASE AND (291 OR 301 OR 97)

=> d l2 ibib ab

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:598143  CAPLUS
DOCUMENT NUMBER:          135:185437
TITLE:                    Aggregate-free urate oxidase for preparation of
                          non-immunogenic polymer conjugates with increased
                          serum persistence
INVENTOR(S):              Sherman, Merry R.; Saifer, Mark G. P.; Williams, L.
                          David
PATENT ASSIGNEE(S):       Mountain View Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 23 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001059078      A2   20010816       WO 2001-US40069  20010207
     WO 2001059078      A3   20020307
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR,
             TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     BR 2001008386      A    20021029       BR 2001-8386     20010207
     EP 1254237         A2   20021106       EP 2001-923265   20010207
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003521937      T2   20030722       JP 2001-558218   20010207
PRIORITY APPLN. INFO.:                   US 2000-501730   A  20000210
```

WO 2001-US40069 W 20010207

AB The invention relates to removal of aggregates larger than octamers from urate oxidases (uricases) prior to conjugation of poly(ethylene glycols) or poly(ethylene oxides). This substantially eliminates **uricase** immunogenicity without compromising its uricolytic activity. Preparative ion-exchange chromatog. of **uricase**, size-exclusion chromatog. of **uricase** monitored by light scattering and UV absorbance, and synthesis of PEG-**uricase** conjugates, are described. In vivo serum persistence and immunogenicity of **uricase** and PEG-**uricase** are studied. Uricolytic activity ELISA assays of PEG-**uricase** in sera from mice injected with PEG-**uricase** are performed. A naturally occurring or recombinant protein, esp. a mutein of **porcine** urate oxidase (**uricase**), that is essentially free of large aggregates can be rendered substantially non-immunogenic by conjugation with a sufficiently small no. of strands of polymer such that the bioactivity of the protein is essentially retained in the conjugate. Such conjugates are unusually well suited for treatment of chronic conditions because they are less likely to induce the formation of antibodies and/or accelerated clearance than are similar conjugates prepd. from protein prepns. contg. traces of large aggregates.

=> s (porcine or pig or hog) and (uricase or urate oxidase) and (291 or 301 or 97)
L3 3 (PORCINE OR PIG OR HOG) AND (URICASE OR URATE OXIDASE) AND (291 OR 301 OR 97)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)

=> d l4 1-3 ibib ab

L4 ANSWER 1 OF 3 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-21416 BIOTECHDS
TITLE: New nucleic acid encoding the human urate transporter (UAT) protein, useful for expressing the protein, which is a potential target for compounds useful for treating disorders characterized by hyperuricemia; vector-mediated uric acid transporter gene transfer and expression in host cell for recombinant protein production and drug screening
AUTHOR: ABRAMSON R G; LEAL-PINTO E; LIPKOWITZ M
PATENT ASSIGNEE: MOUNT SINAI SCHOOL MEDICINE
PATENT INFO: US 6551796 22 Apr 2003
APPLICATION INFO: US 2000-559023 27 Apr 2000
PRIORITY INFO: US 2000-559023 27 Apr 2000; US 1997-70215 31 Dec 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-575996 [54]
AB DERWENT ABSTRACT:
NOVELTY - An isolated nucleic acid (I) encoding a human urate transporter (UAT) protein comprising nucleotides 1-969 of a 972 bp sequence fully defined in the specification, or comprising a nucleotide sequence encoding a **301** amino acid sequence fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a vector (II) comprising (I); (2) a host cell (III) comprising (I) (preferably as (II)); and (3) producing a urate transporter maintaining (III) under conditions in which (I) is expressed to produce the urate transporter.

WIDER DISCLOSURE - The following are disclosed: (1) a fully defined 1545 bp nucleic acid sequence encoding a rat urate transporter; (2) isolated and substantially purified rat and human urate transporters; (3) a pharmaceutical pack or kit comprising at least one composition comprising a compound capable of regulating urate transporter activity.

BIOTECHNOLOGY - Preferred Vector: The vector comprises (I) operably linked to a promoter. Preferred Host Cell: The host cell is a Xenopus oocyte, or a bacterial, yeast, insect or mammalian cell. Isolation: A cDNA for a rat urate transporter was obtained by screening a rat whole kidney cDNA expression library with an affinity purified immunoglobulin G fraction of a polyclonal antiserum to **pig** liver **uricase**

.

ACTIVITY - Nephrotropic; Antianemic; Hypotensive; Cytostatic; Antigout; Litholytic; Anti-HIV; Cardiovascular-gen; Anorectic; Antilipemic; Antidiabetic.

MECHANISM OF ACTION - Urate transporter agonist; Urate transporter antagonist. A block of homology between rat and human urate transporters (UATs) and known copper chaperone proteins was found in searches for local blocks of homology between UATs and known proteins. Based on this finding copper was tested for its ability to modulate recombinant rat and human UAT activity. Increasing ambient copper concentration by adding less than 1 micromolar copper to the bathing solution increased the opening probability for the human UAT from 5-15% to greater than 50-60%, and addition of a similar concentration of a copper chelator (specific compound not stated) almost completely abolished channel activity.

USE - (I) is useful for making a urate transporter, which involves introducing (I) into a host cell (preferably a bacterial, yeast, insect or a mammalian cell), and maintaining the cell under conditions where the nucleic acid is expressed to produce the urate transporter. The method further involves the step of recovering the urate transporter (all claimed). The expressed urate transporter is disclosed as being useful in the identification of agents that agonize or antagonize transporter activity which may be useful for treating diseases or disorders characterized by hyperuricemia, including myeloproliferative disorders, leukemias, chronic hemolytic anemias, multiple myeloma, gout, nephrotoxicity, uric acid stones, HIV, essential hypertension, cardiovascular disease, the metabolic syndrome of obesity, hypertriglyceridemia, glucose intolerance and hypertension (syndrome X), and a form of familial hyperuricemic nephropathy. The urate transporter sequences are useful in computer searching and modelling methods for identification of compounds that modulate transporter activity. Copper and copper compounds are disclosed as being urate channel activators that may be useful in treating disorders characterized by hyperuricemia. Fragments of (I) are useful as hybridization probes for isolating a nucleic acid encoding a urate transporter.

ADVANTAGE - The applicants provide novel nucleic acid sequences for urate transporters which may be useful in identifying compounds useful for treating diseases characterized by hyperuricemia.

EXAMPLE - A rat whole kidney cDNA library (approximately 1.2 x 10 to the power of 6 plaques) unidirectionally cloned in Uni- ZAP XR vector using EcoRI and XhoI at the 5' and 3' ends respectively was screened with an affinity purified immunoglobulin G (IgG) fraction of a polyclonal antibody to **pig** liver **uricase**. A single plaque immunoreactive plaque was detected and a cDNA of 1476 bp was cloned into pBluescript and sequenced. Analysis of the sequence suggested that the first occurring ATG codon was the initiation codon, suggesting a 966 bp open reading frame encoding a 322 amino acid protein with an estimated molecular weight of 36,341 daltons. Database searches with the amino acid sequence suggested that the protein was novel, having no linear sequence homology to **uricase** but having some degree of homology to a family of galactoside binding proteins, the galectins. The predicted protein had the highest degree of homology to galectin 5 (145 amino acids) from rat reticulocytes (Gitt et al. (1995) J Biol Chem 270:5032), with a total of 125 identical amino acids, which are nearly all located in the carboxy terminus of the rat urate transporter.(22 pages)

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:598143 CAPLUS
DOCUMENT NUMBER: 135:185437
TITLE: Aggregate-free **urate oxidase** for

preparation of non-immunogenic polymer conjugates with increased serum persistence
INVENTOR(S): Sherman, Merry R.; Saifer, Mark G. P.; Williams, L. David
PATENT ASSIGNEE(S): Mountain View Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059078	A2	20010816	WO 2001-US40069	20010207
WO 2001059078	A3	20020307		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001008386	A	20021029	BR 2001-8386	20010207
EP 1254237	A2	20021106	EP 2001-923265	20010207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003521937	T2	20030722	JP 2001-558218	20010207

PRIORITY APPLN. INFO.: US 2000-501730 A 20000210
WO 2001-US40069 W 20010207

AB The invention relates to removal of aggregates larger than octamers from urate oxidases (uricases) prior to conjugation of poly(ethylene glycols) or poly(ethylene oxides). This substantially eliminates **uricase** immunogenicity without compromising its uricolytic activity. Preparative ion-exchange chromatog. of **uricase**, size-exclusion chromatog. of **uricase** monitored by light scattering and UV absorbance, and synthesis of PEG-**uricase** conjugates, are described. In vivo serum persistence and immunogenicity of **uricase** and PEG-**uricase** are studied. Uricolytic activity ELISA assays of PEG-**uricase** in sera from mice injected with PEG-**uricase** are performed. A naturally occurring or recombinant protein, esp. a mutein of **porcine urate oxidase** (**uricase**), that is essentially free of large aggregates can be rendered substantially non-immunogenic by conjugation with a sufficiently small no. of strands of polymer such that the bioactivity of the protein is essentially retained in the conjugate. Such conjugates are unusually well suited for treatment of chronic conditions because they are less likely to induce the formation of antibodies and/or accelerated clearance than are similar conjugates prepd. from protein prepns. contg. traces of large aggregates.

L4 ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-05958 BIOTECHDS
TITLE: Recombinant mammalian **uricase** protein used to treat elevated uric acid levels associated with e.g. gout is modified by the insertion of one or more lysine residues; enzyme engineering by substitution of arginine with lysine in **uricase**, used to increase PEG binding to reduce immunogenicity in e.g. gout therapy
AUTHOR: Hershfield M; Kelly S J
PATENT ASSIGNEE: Univ.Duke
LOCATION: Durham, NC, USA.
PATENT INFO: WO 2000008196 17 Feb 2000

APPLICATION INFO: WO 1999-US17678 5 Aug 1999
PRIORITY INFO: US 1998-95489 6 Aug 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-195586 [17]
AB A mammal recombinant **uricase** (EC-1.7.3.3) fusion protein, modified to include one or more lysine residues, is claimed. The fusion protein consists of a 304 amino acid protein sequence containing the N-terminal 225 or 288 amino acids of **pig uricase** (amino acids 1-225 or 1-288 of the **pig** enzyme) and the C-terminal 79 amino acids of baboon **uricase** (amino acid 226-304 or 289-304 of the baboon enzyme), or a given 304, 304, 298, **301**, 298 or **301** amino acid protein sequence. Also claimed is a nucleic acid encoding the **uricase** fusion protein, having a given 915 or 915 bp DNA sequence, a vector containing that sequence and a host cell transformed by the vector. The modified **uricase** have an increased level of available non-deleterious monomethoxypolyethylene glycol (MPEG) attachment sites, increasing MPEG's ability to mask potentially immunogenic epitopes. The proteins can be used to produce improved MPEG-**uricase** conjugates with reduced immunogenicity to treat conditions associated with increased uric acid levels, e.g. gout, organ transplants, kidney insufficiency and malignant disease. The **uricase** is preferably modified by substituting lysine residues for arginine residues. (69pp)

=> s (uricase or urate oxidase) and (291 or 301 or 97)
L5 58 (URICASE OR URATE OXIDASE) AND (291 OR 301 OR 97)

=> s l5 and mammal?
L6 13 L5 AND MAMMAL?

=> dup rem l5 l6
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L6
L7 37 DUP REM L5 L6 (34 DUPLICATES REMOVED)

=> dup rem l6
PROCESSING COMPLETED FOR L6
L8 8 DUP REM L6 (5 DUPLICATES REMOVED)

=> d l8 1-8 ibib ab

L8 ANSWER 1 OF 8 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-21416 BIOTECHDS
TITLE: New nucleic acid encoding the human urate transporter (UAT) protein, useful for expressing the protein, which is a potential target for compounds useful for treating disorders characterized by hyperuricemia;
vector-mediated uric acid transporter gene transfer and expression in host cell for recombinant protein production and drug screening
AUTHOR: ABRAMSON R G; LEAL-PINTO E; LIPKOWITZ M
PATENT ASSIGNEE: MOUNT SINAI SCHOOL MEDICINE
PATENT INFO: US 6551796 22 Apr 2003
APPLICATION INFO: US 2000-559023 27 Apr 2000
PRIORITY INFO: US 2000-559023 27 Apr 2000; US 1997-70215 31 Dec 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
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specification, is new.

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Isolation: A cDNA for a rat urate transporter was obtained by screening a rat whole kidney cDNA expression library with an affinity purified immunoglobulin G fraction of a polyclonal antiserum to pig liver **uricase**.

ACTIVITY - Nephrotropic; Antianemic; Hypotensive; Cytostatic; Antigout; Litholytic; Anti-HIV; Cardiovascular-gen; Anorectic; Antilipemic; Antidiabetic.

MECHANISM OF ACTION - Urate transporter agonist; Urate transporter antagonist. A block of homology between rat and human urate transporters (UATs) and known copper chaperone proteins was found in searches for local blocks of homology between UATs and known proteins. Based on this finding copper was tested for its ability to modulate recombinant rat and human UAT activity. Increasing ambient copper concentration by adding less than 1 micromolar copper to the bathing solution increased the opening probability for the human UAT from 5-15% to greater than 50-60%, and addition of a similar concentration of a copper chelator (specific compound not stated) almost completely abolished channel activity.

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ADVANTAGE - The applicants provide novel nucleic acid sequences for urate transporters which may be useful in identifying compounds useful for treating diseases characterized by hyperuricemia.

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to **uricase** but having some degree of homology to a family of galactoside binding proteins, the galectins. The predicted protein had the highest degree of homology to galectin 5 (145 amino acids) from rat reticulocytes (Gitt et al. (1995) J Biol Chem 270:5032), with a total of 125 identical amino acids, which are nearly all located in the carboxy terminus of the rat urate transporter.(22 pages)

L8 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:336884 BIOSIS
DOCUMENT NUMBER: PREV200300336884
TITLE: Recombinant **Urate Oxidase** (Rasburicase) Is Safe and Effective in Managing Hyperuricemia in Children and Adults: Results of a Multi-National Compassionate Use Trial.
AUTHOR(S): Bosly, Andre (1); Pinkerton, C. Ross (1); McCowage, Geoffrey (1); Bron, Dominique (1); Sanz, Miguel A. (1); Van den Berg, Hendrik (1)
CORPORATE SOURCE: (1) Cliniques Universitaires, Mont-Godinne, Belgium Belgium
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11 , pp. Abstract No. 2187. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Hyperuricemia and tumor lysis syndrome (TLS) remain significant issues in the treatment of adults and children with haematological malignancies, despite standard management with allopurinol and alkalinization. Rasburicase (ElitekTM, Fasturtec(R)), a recombinant **urate oxidase**, that converts uric acid (UA) into soluble allantoin, has been demonstrated to control hyperuricemia faster and more reliably than allopurinol (Goldman et al Blood 2001). A compassionate use trial provided access to rasburicase for patients at risk of TLS during initiation chemotherapy in 9 countries from 01/1999 to 12/2001. 166 pediatric patients (median age 6, range 0.1 - 17) with leukemia (74 %), predominantly pre-B-cell ALL (34 %), T-cell ALL (19 %) and AML (8 %), and with lymphoma (24 %), mainly Burkitt's (13 %), as well as with solid tumors (3 %) were included. The study also included 112 adults (median age 54, range 18 - 80) with leukemia (68 %), predominantly AML (38 %), pre-B-cell ALL (10 %) and blast crises of CML (8 %), and with lymphoma (26 %). Rasburicase (0.20 mg/kg) was administered intravenously daily for 1 to 7 days at the investigator's discretion. Two doses daily could be given during the initial 3 days. Both adult and pediatric patients who were hyperuricemic at presentation received a median of 6 doses (range 1-24 in children; 1-10 in adults) whereas for prophylaxis in non-hyperuricemic adults and children a median of 5 doses (range 1-13 in children; 1-10 in adults) were used. UA levels 24 - 48 hours after the last dose of rasburicase were available for 122 pediatric and **97** adult patients. The mean UA levels in 29 hyperuricemic children decreased from 15.1 mg/dL (STD 8.3) to 0.8 mg/dL (STD 2.5) ($p<0.001$) after treatment, whereas in 27 hyperuricemic adults the reduction was from 14.2 mg/dL (STD 5.7) to 0.5 mg/dL (STD 0.7) ($p<0.001$). In 93 non-hyperuricemic children who received prophylactic rasburicase to prevent TLS during chemotherapy UA levels were reduced from a mean of 4.4 mg/dL (STD 1.8) to 0.8 mg/dL (STD 0.9) ($p<0.001$). Prophylactic treatment of 70 non-hyperuricemic adults decreased mean uric acid from 4.8 mg/dL (STD 1.5) to 0.4 mg/dL (STD 0.3) ($p<0.001$). A response was defined as a reduction/maintenance of UAltoreq7.5 mg/dL (ltoreq6.5 mg/dL in children < 13). The only non-responder was a 2-month old male with early pre-B-cell ALL, whose UA level decreased from 21.9 mg/dL to 13.5 mg/dL after 10 doses of rasburicase. Response rate was thus 96.6 % in hyperuricemic children and 100 % in non-hyperuricemic children and in adults. Three pediatric and one adult patient received dialysis to manage acute renal failure, in spite of rasburicase reducing UA levels to within or below the normal range. Two of

these patients died, one due to progressive disease and dyspnoea and the other due to progressive disease, respiratory failure and acute renal failure. Rasburicase was very well tolerated. Drug-related SAEs were only observed in one patient - a grade 2 allergic reaction with a grade 1 fever in a 36 year old male AML patient who recovered without sequelae upon discontinuation of rasburicase and administration of paracetamol. The results confirm that rasburicase is safe and highly effective in the prevention and treatment of chemotherapy induced hyperuricemia in both children and adults.

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:598143 CAPLUS
DOCUMENT NUMBER: 135:185437
TITLE: Aggregate-free **urate oxidase** for preparation of non-immunogenic polymer conjugates with increased serum persistence
INVENTOR(S): Sherman, Merry R.; Saifer, Mark G. P.; Williams, L. David
PATENT ASSIGNEE(S): Mountain View Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059078	A2	20010816	WO 2001-US40069	20010207
WO 2001059078	A3	20020307		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001008386	A	20021029	BR 2001-8386	20010207
EP 1254237	A2	20021106	EP 2001-923265	20010207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003521937	T2	20030722	JP 2001-558218	20010207

PRIORITY APPLN. INFO.: US 2000-501730 A 20000210
WO 2001-US40069 W 20010207

AB The invention relates to removal of aggregates larger than octamers from urate oxidases (uricases) prior to conjugation of poly(ethylene glycols) or poly(ethylene oxides). This substantially eliminates **uricase** immunogenicity without compromising its uricolytic activity. Preparative ion-exchange chromatog. of **uricase**, size-exclusion chromatog. of **uricase** monitored by light scattering and UV absorbance, and synthesis of PEG-**uricase** conjugates, are described. In vivo serum persistence and immunogenicity of **uricase** and PEG-**uricase** are studied. Uricolytic activity ELISA assays of PEG-**uricase** in sera from mice injected with PEG-**uricase** are performed. A naturally occurring or recombinant protein, esp. a mutein of porcine **urate oxidase** (**uricase**), that is essentially free of large aggregates can be rendered substantially non-immunogenic by conjugation with a sufficiently small no. of strands of polymer such that the bioactivity of the protein is essentially retained in the conjugate. Such conjugates are unusually well suited for treatment of chronic conditions because they are less likely to induce the formation of antibodies and/or accelerated clearance than are similar conjugates

prepd. from protein prepns. contg. traces of large aggregates.

L8 ANSWER 4 OF 8 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-05958 BIOTECHDS
TITLE: Recombinant **mammalian uricase** protein used to treat elevated uric acid levels associated with e.g. gout is modified by the insertion of one or more lysine residues;
enzyme engineering by substitution of arginine with lysine in **uricase**, used to increase PEG binding to reduce immunogenicity in e.g. gout therapy
AUTHOR: Hershfield M; Kelly S J
PATENT ASSIGNEE: Univ.Duke
LOCATION: Durham, NC, USA.
PATENT INFO: WO 2000008196 17 Feb 2000
APPLICATION INFO: WO 1999-US17678 5 Aug 1999
PRIORITY INFO: US 1998-95489 6 Aug 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-195586 [17]
AB A **mammal** recombinant **uricase** (EC-1.7.3.3) fusion protein, modified to include one or more lysine residues, is claimed. The fusion protein consists of a 304 amino acid protein sequence containing the N-terminal 225 or 288 amino acids of pig **uricase** (amino acids 1-225 or 1-288 of the pig enzyme) and the C-terminal 79 amino acids of baboon **uricase** (amino acid 226-304 or 289-304 of the baboon enzyme), or a given 304, 304, 298, **301**, 298 or **301** amino acid protein sequence. Also claimed is a nucleic acid encoding the **uricase** fusion protein, having a given 915 or 915 bp DNA sequence, a vector containing that sequence and a host cell transformed by the vector. The modified **uricase** have an increased level of available non-deleterious monomethoxypolyethylene glycol (MPEG) attachment sites, increasing MPEG's ability to mask potentially immunogenic epitopes. The proteins can be used to produce improved MPEG-**uricase** conjugates with reduced immunogenicity to treat conditions associated with increased uric acid levels, e.g. gout, organ transplants, kidney insufficiency and malignant disease. The **uricase** is preferably modified by substituting lysine residues for arginine residues. (69pp)

L8 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:341430 BIOSIS
DOCUMENT NUMBER: PREV199800341430
TITLE: Amperometric biosensor for uric acid based on **uricase**-immobilized silk fibroin membrane.
AUTHOR(S): Zhang, Yu-Qing (1); Chen, Wei-De; Gu, Ren-Ao; Zhu, Jiang; Xue, Ren-Yu
CORPORATE SOURCE: (1) Biotechnol. Lab. Silkworm Silk, Sch. Seric., Suzhou Univ., Suzhou 215151 China
SOURCE: Analytica Chimica Acta, (Aug. 10, 1998) Vol. 369, No. 1-2, pp. 123-128.
ISSN: 0003-2670.
DOCUMENT TYPE: Article
LANGUAGE: English
AB An amperometric urate sensor based on a **uricase**-immobilized silk fibroin membrane and an oxygen electrode in flow injection analysis are described in the present paper. The biosensor shows that recoveries of uric acid in human serum and urine are in the range of 94.2-102.6% and 92.5-**97**.9%, respectively. The relative standard deviations (RSDs) for repeatedly monitoring standard urate solution, human serum and urine are 2.37, 3.72 and 2.95%, respectively, based on 100 measurements. The urate sensor based on the **uricase**-immobilized membrane is capable of detecting 60-70 human serum samples per hour. Moreover, a piece of **uricase**-immobilized fibroin membrane used at the sensor could not only be stored for over 2 years, but also repeatedly monitored more

than 1000 times for biosamples such as human serum or urine.

L8 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:222645 BIOSIS
DOCUMENT NUMBER: PREV199800222645
TITLE: Reference values of common blood chemistry analytes in healthy population of Rawalpindi-Islamabad area.
AUTHOR(S): Khan, Farooq Ahmad; Dilawa, Muhammad; Khan, Dilshad Ahmad
CORPORATE SOURCE: Dep. Chem. Pathol. Endocrinol., Armed Forces Inst. Pathol., Rawalpindi Pakistan
SOURCE: JPMA (Journal of the Pakistan Medical Association), (June, 1997) Vol. 47, No. 6, pp. 156-159.
ISSN: 0030-9982.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The reference values of common blood chemistry analytes in healthy population, aged newborn to 80 years, of Rawalpindi Islamabad area were determined at AFIP, Rawalpindi. A total of 2115 healthy subjects, 1206 males and 909 females, were included in the study. Plasma glucose was analysed by GOD/POD, serum cholesterol by CHOD/PAP, triglycerides by GPO/PAP, urea by urease/GLDH, creatinine by Jaffe' rate reaction, uric acid by **uricase**, total bilirubin by Jendrassik and Grof, total protein by biuret, alanine transaminase (ALT) by optimized IFCC and alkaline phosphatase (AP) by optimized DGKC method. The between batch CVs of all the parameters were within acceptable quality goals. The reference values were calculated using 2.5 and **97**.5 percentiles as lower and upper limits (95% CI). In healthy adult males the reference values were: fasting plasma glucose, 3.6-6.0 mmol/l; serum cholesterol; 3.2-6.6 mmol/l; triglycerides, 0.6-2.3 mmol/l, urea, 2.8-6.4 mmol/l; creatinine, 65-132 umol/l; uric acid, 164-430 umol/l; total bilirubin, 5-18 umol/l, total protein, 57-83 g/l; ALT, 15-45 U/l and AP, 185-620 U/l. The values in adult females, children and elderly subjects were slightly different than adult males. The reference values of our population show mild to moderate differences from the other Asian, European and American populations. It is recommended that reference values of different biochemical investigations should be established in various areas of Pakistan to make appropriate use of such investigations.

L8 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 89057880 MEDLINE
DOCUMENT NUMBER: 89057880 PubMed ID: 3194410
TITLE: Isolation and sequence determination of a cDNA clone for rat peroxisomal **urate oxidase**: liver-specific expression in the rat.
AUTHOR: Reddy P G; Nemali M R; Reddy M K; Reddy M N; Yuan P M; Yuen S; Laffler T G; Shiroza T; Kuramitsu H K; Usuda N; +
CORPORATE SOURCE: Department of Pathology, Northwestern University Medical School, Chicago, IL 60611.
CONTRACT NUMBER: R37 GM 23750 (NIGMS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 Dec) 85 (23) 9081-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X13098
ENTRY MONTH: 198812
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881230
AB **Urate oxidase** (UOxase; urate:oxygen oxidoreductase, EC 1.7.3.3), which catalyzes the oxidation of uric acid to allantoin, is present in most **mammals** but is absent in humans and certain primates. A cDNA clone for UOxase containing an insert of 1.3 kilobases

(kb) was isolated from a lambda gt11 cDNA library prepared from rat liver mRNA. This recombinant clone with a 1283-nucleotide insert has sequence for **97%** of the coding region together with 401 nucleotides of the 3'-untranslated region of the mRNA. The identity of UOxase cDNA clone was verified by analyzing the fusion protein, immunocytochemical localization with epitope-selected antibody, and hybrid-select translation analysis and by comparing sequences of four CNBr-cleaved peptides of the protein. Blot analysis revealed that the probe hybridizes to a single 1.5-kb mRNA species in the rat liver and a transplantable hepatocellular carcinoma. No UOxase mRNA was detected in 11 nonhepatic tissues of rat, suggesting tissue specificity of expression of this UOxase gene. Blot analysis of RNA from livers of rats treated with a peroxisome proliferator showed 2- to 3-fold increase in UOxase mRNA content, whereas the fatty acyl-CoA oxidase mRNA increased over 30-fold. Southern blot analysis of restriction enzyme digests of rat DNA suggests that there is a single copy of UOxase gene. Analysis of human genomic DNA revealed restriction fragments that are homologous to rat UOxase cDNA, although no UOxase mRNA was detected in human liver.

L8 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 86192526 MEDLINE
DOCUMENT NUMBER: 86192526 PubMed ID: 3009190
TITLE: Isolation and characterization of peroxisomes from the renal cortex of beef, sheep, and cat.
AUTHOR: Zaar K; Volkl A; Fahimi H D
SOURCE: EUROPEAN JOURNAL OF CELL BIOLOGY, (1986 Mar) 40 (1) 16-24. Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198606
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860609

AB The isolation and characterization of highly purified and structurally well-preserved peroxisomes from the renal cortex of different **mammalian** species (beef, sheep, and cat) is reported. Renal cortex tissue was homogenized and a peroxisome-enriched light mitochondrial fraction was prepared by differential centrifugation. This was subfractionated by density-dependent banding on a linear gradient of metrizamide (1.12-1.26 g/cm3) using a Beckman VTi 50 vertical rotor. Peroxisomes banded at a mean density of 1.225 cm3. Ultrastructural morphometric examination revealed that peroxisomes made up **97** to 98% of the isolated fractions. By biochemical analysis the contamination with marker enzymes of mitochondria and lysosomes was extremely low. The specific activity of catalase was enriched, depending on the species, between 28- and 38-fold over the homogenate. Peroxisome preparations from all three species exhibited a high but varying level of activity for cyanide-insensitive lipid beta-oxidation. In beef and sheep preparations a small amount of esterase activity cosediments with peroxisomes. These peroxisomes show distinct structural membrane associations with smooth elements of ER. **Urate oxidase**, a marker enzyme for rat liver peroxisomes, is found only in peroxisomes prepared from beef kidney cortex, with sheep and cat preparations being negative. This correlated with the occurrence of polytubular inclusions in the beef kidney peroxisomes. The large size and the angular shape of isolated peroxisomes as well as the presence of paracrystalline matrical inclusions imply that the majority of peroxisomes are derived from the epithelial cells of the proximal tubule of the kidney cortex. The significant differences found in the characteristics of the renal peroxisomes in three different species investigated, demonstrate the remarkable adaptability and plasticity of this organelle.

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=> s  (uricase or urate oxidase) and ovine
L9            1 (URICASE OR URATE OXIDASE) AND OVINE

=> d l9

L9    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AN    2002-00996  BIOTECHDS
TI    Purified urate-oxidase substantially free of
      aggregates larger than octamers useful for treating elevated uric acid
      levels associated gout, tophi, renal insufficiency, organ transplantation
      and malignant disease;
         human, pig liver, fungus, plant recombinant uricase useful
         in disease therapy
AU    Sherman M R; Saifer M G P; Williams L D
PA    Mountain-View-Pharmaceuticals
LO    Menlo Park, CA, USA.
PI    WO 2001059078 16 Aug 2001
AI    WO 2001-US40069 7 Feb 2001
PRAI  US 2000-501730 10 Feb 2000
DT    Patent
LA    English
OS    WPI: 2001-570528 [64]


=> d l9 ab

L9    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AB    A purified urate-oxidase (uricase
      (EC-1.7.3.3)) (I) substantially free of aggregates larger than octamers,
      is claimed.  (I) is a mammalian uricase, or pig liver, cattle
      liver, ovine liver or baboon liver uricase, fungal
      uricase, microbial uricase or plant uricase.
      (I) is a recombinant or chimeric uricase.  Also claimed are: a
      pharmaceutical composition (II) for lowering uric acid levels in the body
      fluid or tissue; purification (M) of (I) having reduced immunogenicity,
      involves separating uricase aggregates larger than octamers in
      uricase fractions, where the separation is performed by
      ionexchange chromatography, size-exclusion chromatography or
      ultrafiltration, and excluding the aggregates from the purified
      uricase; and an isolated uricase (III) prepared by (M).
      (II) is useful for lowering the levels of uric acid in a body fluid or
      tissue of humans and for treating elevated uric acid levels associated
      with conditions including gout, tophi, renal insufficiency, organ
      transplantation and malignant disease.  (23pp)


=> s  (uricase or urate oxidase) and bovine
L10          107 (URICASE OR URATE OXIDASE) AND BOVINE

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           69 DUP REM L10 (38 DUPLICATES REMOVED)

=> focus l11
PROCESSING COMPLETED FOR L11
L12           69 FOCUS L11 1-

=> s l12 and dna
L13           2 L12 AND DNA

=> d l13 1-2 ibib ab

L13  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:906205  CAPLUS
DOCUMENT NUMBER:          136:42809
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TITLE: Method for nucleic acid transfection of cells using cationic lipid/**DNA** complex
INVENTOR(S): Bennett, Michael J.; Rothman, Stephan S.; Nantz, Michael H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U. S. Ser. No. 487,089.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001051610	A1	20011213	US 2001-766320	20010118
US 6372722	B1	20020416	US 2000-487089	20000119
WO 2001052903	A1	20010726	WO 2001-US1803	20010119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1250156	A1	20021023	EP 2001-908634	20010119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003520253	T2	20030702	JP 2001-552950	20010119

PRIORITY APPLN. INFO.:
US 2000-487089 A2 20000119
US 2001-766320 A 20010118
WO 2001-US1803 W 20010119

AB The present invention describes methods for introducing nucleic acids into a target cell using a transition metal enhancer. A mixt. contg. nucleic acid and a transition metal enhancer is exposed to cells. The nucleic acid is taken up into the interior of the cell with the aid of the transition metal enhancer. The transition metal enhancer tested includes zinc, nickel, cobalt and copper in animal cell line, or rat salivary gland or mouse lung. It is shown zinc can enhance both in vitro and in vivo transfection of liposome/**DNA** mixt. depending on the cationic lipid to nucleic acid charge ratio. Since nucleic acids can encode a gene, the method can be used to replace a missing or defective gene in the cell. The method can also be used to deliver exogenous nucleic acids operatively coding for proteins that are secreted or released from target cells, thus resulting in a desired biol. effect outside the cell. Alternatively, the methods of the present invention can be used to deliver exogenous nucleic acids into a target cell that are capable of regulating the expression of a predetd. endogenous gene. This can be accomplished by encoding the predetd. endogenous gene on the nucleic acid or by encoding the nucleic acid with a sequence that is the Watson-Crick complement of the mRNA corresponding to the endogenous gene.

L13 ANSWER 2 OF 2 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 96224455 EMBASE
DOCUMENT NUMBER: 1996224455
TITLE: Pharmacokinetics and targeted delivery of proteins and genes.
AUTHOR: Hashida M.; Mahato R.I.; Kawabata K.; Miyao T.; Nishikawa M.; Takakura Y.
CORPORATE SOURCE: Department of Drug Delivery Research, Faculty of Pharmaceutical Sciences, Kyoto University,Sakyo-ku, Kyoto 606-01, Japan
SOURCE: Journal of Controlled Release, (1996) 41/1-2 (91-97).

ISSN: 0168-3659 CODEN: JCREEC
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 022 Human Genetics
023 Nuclear Medicine
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effectiveness of various approaches for controlling in vivo disposition of proteins and genes was compared based on pharmacokinetic analysis. The potential of introduction of galactose or mannose residues aiming at receptor-mediated endocytosis, succinylation to be recognized by a scavenger receptor, and cationization for universal electrostatic interaction were characterized using model proteins. Corresponding to the results, a superior therapeutic effect was shown with derivatives of superoxide dismutase against hepatic and renal ischemia/reperfusion injury. A similar approach was adopted for plasmid **DNA** and oligonucleotide and their rapid degradation in the blood pool and preferential uptake by the liver after intravenous injection were characterized by pharmacokinetic analysis. The effects of incorporation into cationic liposomes and conjugation with macromolecules on their in vivo distribution were also elucidated.

=> d l12 1-5 ibib ab

L12 ANSWER 1 OF 69 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1970:62994 CAPLUS
DOCUMENT NUMBER: 72:62994
TITLE: Effect of guanidine derivatives on **urate oxidase** activity
AUTHOR(S): Bentley, Keith W.; Truscoe, Richard
CORPORATE SOURCE: Dep. Biochem., Victoria Univ., Wellington, N. Z.
SOURCE: Enzymologia (1969), 37(5-6), 285-313
CODEN: ENZYAS; ISSN: 0013-9424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Bovine** kidney **urate oxidase** (EC 1.7.3.3) was progressively and irrever sibly inactivated by incubation with guanidinium salts and biguanide salts at concns. of 10-100mM. Dicyandiamide had a weaker and possibly reversible action at these concns. The inactivating effect was pH-dependent and increased very rapidly at pH levels >10, suggesting that the effect is due to deprotonation of lysine .epsilon.-amino groups followed by reaction with a guanidinium ion. The inactivating effect may be also due to formation of stable chelates with a Cu atom at the enzyme catalytic center. Guanidinium chloride, guanidinium carbonate, and guanidinium sulfate in various grades of purity showed no significant differences in action, indicating that inhibitory effects obsd. could not be attributed to the presence of any very active minor impurities as had been shown by Fridovich for inhibition of xanthine oxidase. Hibitane (hexamethylene-1,6-bis[1-(5-p-chlorophenyl)biguanidine acetate] significantly inactivated at doses as low as 0.05mM and total inactivation at <1mM was also pH dependent. Arginine weakly inactivated the enzyme, showing a pH dependence similar to that obsd. with other guanidine derivs. Creatine and creatinine at 10-100mM were ineffective. N-Eth-ylmaleimide was a powerful inactivator of **urate oxidase** and showed similar pH-dependent action, with a sharp increase in sensitivity of the enzyme at pH levels >10. This supports the view that lysine is a component of the **urate oxidase** cat alytic site.

L12 ANSWER 2 OF 69 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:522030 CAPLUS
DOCUMENT NUMBER: 71:122030
TITLE: Effect of streptomycin on **urate oxidase** activity
AUTHOR(S): Rainforth, T. D.; Truscoe, R.
CORPORATE SOURCE: Victoria Univ., Wellington, N. Z.
SOURCE: Enzymologia (1969), 37(3), 185-96
CODEN: ENZYAS; ISSN: 0013-9424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Streptomycin sulfate (3mM) incubated with exts. of the mitochondrial fraction of the **bovine** renal cortex in 0.2M ammonia at pH 10.25 and 37.degree. caused unselective pptn. of 50% of the protein and 100% inactivation of **urate oxidase** (EC 1.7.3.3). Protein pptn. and enzyme inactivation did not occur when Tris was substituted for ammonia. The processes were markedly pH-dependent, the fall in activity and in protein increasing linearly in ammonia systems contg. 1.5 mM streptomycin as the pH was raised from 8.5 to 10.25. The rate of protein pptn. was much faster than that of enzyme inactivation, indicating that the 2 processes were sep. Phosphate at concns. >0.02M abolished protein pptn. but did not affect inactivation of **urate oxidase** by streptomycin. The enzyme inactivating activity of streptomycin was not reversed by prolonged dialysis against 0.2M ammonia or by treatment with 0.5% Tamol 731.

L12 ANSWER 3 OF 69 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:96165 CAPLUS
DOCUMENT NUMBER: 76:96165
TITLE: Immunoenzymology of purified **urate oxidase**
AUTHOR(S): Fitzpatrick, D. A.; Fitzgerald, O.; McGeeney, K. F.
CORPORATE SOURCE: Dep. Med. Ther., Univ. Coll., Dublin, Ire.
SOURCE: Biochemical Journal (1971), 125(4), 114p
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purified prepns. of **urate oxidase** (I) from pig liver (EC 1.7.3.3) were used to immunize both guinea pigs and rabbits. The antisera were tested for cross-reaction with I prepd. from other sources. Reactions of complete identity were obtained with I from **bovine** kidney and partial identity with I from Rhombus maximus and Pleuronectes platessa, but complete failure to react with I from various microbial sources was obsd. When I from mammalian and microbial sources was heated at 50.degree. for 10 min and at 70.degree. for 30 min, and the antigenic integrity compared with unheated controls, I from pig liver and from yeast differed from fungal I by giving a precipitin line on immunodiffusion after heating at the lower temp., but bacterial I differed from all 3 by giving a pos. result after heating at either temp.

L12 ANSWER 4 OF 69 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:498431 CAPLUS
DOCUMENT NUMBER: 71:98431
TITLE: Effects of treatment with dithiothreitol on the extraction, activity and purification of ox-kidney **urate oxidase**
AUTHOR(S): James, K. A. C.; Tate, W. P.; Truscoe, R.
CORPORATE SOURCE: Victoria Univ. Wellington, Wellington, N. Z.
SOURCE: Enzymologia (1969), 37(2), 131-52
CODEN: ENZYAS; ISSN: 0013-9424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ox kidney **urate oxidase** (UO) exts. were highly purified by gel filtration of solns. of (NH4)2SO4-pptd. enzyme previously incubated with 10mM dithiothreitol (DTT). This sepd. the enzyme into 2

fractions, 1 emerging with the single protein peak (peak I) and the other following soon after (peak II). The specific activity of the enzyme of peak II was .apprx.30-fold greater than was that of the initial ext. The peak II enzyme had a mol. wt. of .apprx.100,000, by a gel-filtration method and by a sedimentation method. The Km values of peaks I and II fractions were the same, i.e. 1.75 .times.105; this value is close to those reported by other authors for pig liver and housefly UO. incubation of exts. with deoxycholate led to formation of products of lower mol. wt., which emerged from the columns together with enzyme, no useful sepn. of inert from active protein being achieved. Reincubation of peak I UO with DTT, or treatment with deoxycholate, failed to yield further peak II fractions; it is concluded that if the UO of this fraction is bound to inert protein, SS bridges or hydrophobic binding forces are not concerned. Alk. exts. of acetone powders of the mitochondrial fraction of **bovine** kidney cortex evidently contain 2 forms of UO, one of which is separable from 95% of the protein of the exts. by gel filtration through Sephadex G-200, following preincubation with 5-10mM DTT.

L12 ANSWER 5 OF 69 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:418945 CAPLUS
DOCUMENT NUMBER: 89:18945
TITLE: Affinity chromatography of **urate oxidase** on 8-aminoxanthine-bound Sepharose
AUTHOR(S): Watanabe, Takafumi; Suga, Tetsuya
CORPORATE SOURCE: Dep. Clin. Biochem., Tokyo Coll. Pharm., Tokyo, Japan
SOURCE: Analytical Biochemistry (1978), 86(2), 357-62
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An agarose deriv. that is an affinity adsorbent for chromatog. of **urate oxidase** was prepd. by coupling 8-aminoxanthine with epoxy-activated Sepharose 4B. This affinity adsorbent was stable in 0.1M borate buffer (pH 10.0) at 4.degree.. Chromatog. of crude urate oxidases prepd. from **bovine** kidney, rat liver, and yeast on the affinity column resulted in 2- to 88-fold purifns.

=> d his

(FILE 'HOME' ENTERED AT 11:11:41 ON 10 SEP 2003)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, BIOTECHDS' ENTERED AT 11:12:27 ON 10 SEP 2003

L1 0 S PORCINE URICASE AND (291 OR 301 OR 97)
L2 1 S PORCINE AND URICASE AND (291 OR 301 OR 97)
L3 3 S (PORCINE OR PIG OR HOG) AND (URICASE OR URATE OXIDASE) AND (2
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)
L5 58 S (URICASE OR URATE OXIDASE) AND (291 OR 301 OR 97)
L6 13 S L5 AND MAMMAL?
L7 37 DUP REM L5 L6 (34 DUPLICATES REMOVED)
L8 8 DUP REM L6 (5 DUPLICATES REMOVED)
L9 1 S (URICASE OR URATE OXIDASE) AND OVINE
L10 107 S (URICASE OR URATE OXIDASE) AND BOVINE
L11 69 DUP REM L10 (38 DUPLICATES REMOVED)
L12 69 FOCUS L11 1-
L13 2 S L12 AND DNA

=> s (uricase or urate oxidase) and (dna or rna or nucleic acid) and tyrosine 97
2 FILES SEARCHED...
L14 0 (URICASE OR URATE OXIDASE) AND (DNA OR RNA OR NUCLEIC ACID) AND TYROSINE 97

=> s (uricase or urate oxidase) and (dna or rna or nucleic acid) and (mutation or variant
2 FILES SEARCHED...
L15 62 (URICASE OR URATE OXIDASE) AND (DNA OR RNA OR NUCLEIC ACID) AND

(MUTATION OR VARIANT OR MUTANT)

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 40 DUP REM L15 (22 DUPLICATES REMOVED)

=> focus l16
PROCESSING COMPLETED FOR L16
L17 40 FOCUS L16 1-

=> d l17 1-10 ibib ab

L17 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:418659 CAPLUS
DOCUMENT NUMBER: 113:18659
TITLE: **Urate oxidase**: primary structure and evolutionary implications
AUTHOR(S): Wu, Xiangwei; Lee, Cheng Chi; Muzny, Donna M.; Caskey, C. Thomas
CORPORATE SOURCE: Verna and Marrs McLean Dep. Biochem., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1989), 86(23), 9412-16
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Urate oxidase**, or **uricase** (EC 1.7.3.3), is a peroxisomal enzyme that catalyzes the oxidn. of uric acid to allantoin in most mammals. In humans and certain other primates, however, the enzyme has been lost by some unknown mechanism. To identify the mol. basis for this loss, **urate oxidase** cDNA clones were isolated from pig, mouse, and baboon, and their **DNA** sequences were detd. The mouse **urate oxidase** open reading frame encodes a 303-amino acid polypeptide, while the pig and baboon **urate oxidase** cDNAs encode a 304-amino acid polypeptide due to a single codon deletion/insertion event. The authenticity of this single addnl. codon was confirmed by sequencing the mouse and pig genomic copies of the gene. The **urate oxidase** sequence contains a domain similar to the type 2 copper binding motif found in other copper binding proteins, suggesting that the copper ion in **urate oxidase** is coordinated as a type 2 structure. Based upon a comparison of the NH2-terminal peptide and deduced sequences, it is proposed that the maturation of pig **urate oxidase** involves the posttranslational cleavage of a 6-amino acid peptide. Two nonsense mutations were found in the human **urate oxidase** gene, which confirms, at the mol. level, that the **urate oxidase** gene in humans is nonfunctional. The sequence comparisons favor the hypothesis that the loss of **urate oxidase** in humans is due to a sudden mutational event rather than a progressive mutational process.

L17 ANSWER 2 OF 40 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1997-06396 BIOTECHDS
TITLE: **Mutant uricase**, **mutant uricase** gene, novel recombinant **DNA**, and production of **mutant uricase**; enzyme engineering, and gene cloning and expression in Escherichia coli, for use in uric acid determination and clinical diagnosis
PATENT ASSIGNEE: Kikkoman
LOCATION: Japan.
PATENT INFO: JP 09056383 4 Mar 1997
APPLICATION INFO: JP 1995-216239 24 Aug 1995
PRIORITY INFO: JP 1995-216239 24 Aug 1995
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
OTHER SOURCE: WPI: 1997-206630 [19]
AB A new **mutant uricase** (EC-1.7.3.3) **DNA** sequence encodes a specified protein sequence, with amino acids 165-170 mutated. The **DNA** may be inserted in a vector for expression of recombinant **mutant uricase** in Escherichia coli. The mutated sequence is preferably FIRDEY. Plasmid pUO1001 containing the **uricase** gene has been produced from plasmid pUOX101 (FERM BP-3842), and has been used for in vitro mutagenesis in E. coli XL1-Blue (FERM BP-5204). The enzyme is useful in clinical diagnosis for specific quantification of uric acid in serum or urine. The **mutant** enzyme is physically and chemically stable, as compared with conventional **uricase**, which is easily inactivated on storage.

L17 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:642704 CAPLUS
DOCUMENT NUMBER: 119:242704
TITLE: Characterization, cloning and integrative properties of the gene encoding **urate oxidase** in Aspergillus nidulans
AUTHOR(S): Oestreicher, Nathalie; Sealy-Lewis, Heather M.; Scazzocchio, Claudio
CORPORATE SOURCE: Inst. Genet. Microbiol., Univ. Paris-Sud, Orsay, 91405, Fr.
SOURCE: Gene (1993), 132(2), 185-92
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A no. of mutations were obtained which define the structural gene (uaZ) coding for **urate oxidase** in linkage group I of Aspergillus nidulans. This gene was cloned by transformation of a uaZ- null **mutant**. A chromosome I/VIII translocation which splits the gene was defined both genetically and phys. All known mutations are contained in a 1-kb fragment, itself contained in the probe which recognizes a 1.2-kb inducible message. Plasmids carrying uaZ show a strict bias towards homologous recombination in transformation expts.

L17 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of **nucleic acid** probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L17 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:828415 CAPLUS
DOCUMENT NUMBER: 137:89412
TITLE: Detection of variations in the **DNA** methylation profile of genes in the determining the risk of disease
INVENTOR(S): Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PATENT ASSIGNEE(S): Epigenomics A.-G., Germany
SOURCE: PCT Int. Appl., 636 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 68
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077373	A2	20011018	WO 2001-XA1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
DE 10019058	A1	20011220	DE 2000-10019058	20000406
WO 2001077373	A2	20011018	WO 2001-DE1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1274865	A2	20030115	EP 2001-953936	20010406
R: AT, BE, CH, DE, DK, ES; FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003162194	A1	20030828	US 2003-240452	20030414

PRIORITY APPLN. INFO.: DE 2000-10019058 A 20000406
WO 2001-DE1486 W 20010406

DE 2000-10019173 A 20000407
DE 2000-10032529 A 20000630
DE 2000-10043826 A 20000901
WO 2001-EP3969 W 20010406

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the **DNA** methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene **variant** with regard to **DNA** methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or sexual dysfunction. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

L17 ANSWER 6 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:123837 BIOSIS
DOCUMENT NUMBER: PREV200200123837
TITLE: **Mutant uricase**, a **mutant** **uricase** gene, a novel recombinant **DNA**, and a process for producing **mutant** **uricase**.
AUTHOR(S): Koyama, Y.; Ichikawa, T.
CORPORATE SOURCE: Noda Japan
ASSIGNEE: KIKKOMAN CORPORATION
PATENT INFORMATION: US 5801036 Sept. 1, 1998
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sept. 1, 1998) Vol. 1214, No. 1, pp. 561. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L17 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:88202 BIOSIS
DOCUMENT NUMBER: PREV200200088202
TITLE: **Mutant uricase**, a **mutant** **uricase** gene, a novel recombinant **DNA**, and a process for producing **mutant** **uricase**.
AUTHOR(S): Koyama, Y.; Ichikawa, T.
CORPORATE SOURCE: Noda Japan
ASSIGNEE: KIKKOMAN CORPORATION
PATENT INFORMATION: US 5700674 Dec. 23, 1997
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 23, 1997) Vol. 1205, No. 4, pp. 3029. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L17 ANSWER 8 OF 40 MEDLINE on STN
ACCESSION NUMBER: 92211724 MEDLINE
DOCUMENT NUMBER: 92211724 PubMed ID: 1556746
TITLE: Two independent mutational events in the loss of **urate oxidase** during hominoid evolution.

AUTHOR: Wu X W; Muzny D M; Lee C C; Caskey C T
CORPORATE SOURCE: Verna and Marrs McLean Department of Biochemistry, Baylor College of Medicine, Houston, TX 77030.
CONTRACT NUMBER: DK31428 (NIDDK)
SOURCE: JOURNAL OF MOLECULAR EVOLUTION, (1992 Jan) 34 (1) 78-84. Journal code: 0360051. ISSN: 0022-2844.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920515
Last Updated on STN: 19980206
Entered Medline: 19920505

AB **Urate oxidase** was lost in hominoids during primate evolution. The mechanism and biological reason for this loss remain unknown. In an attempt to address these questions, we analyzed the sequence of **urate oxidase** genes from four species of hominoids: human (Homo sapiens), chimpanzee (Pan troglodytes), orangutan (Pongo pygmaeus), and gibbon (Hylobates). Two nonsense mutations at codon positions 33 and 187 and an aberrant splice site were found in the human gene. These three deleterious mutations were also identified in the chimpanzee. The nonsense **mutation** at codon 33 was observed in the orangutan **urate oxidase** gene. None of the three mutations was present in the gibbon; in contrast, a 13-bp deletion was identified that disrupted the gibbon **urate oxidase** reading frame. These results suggest that the loss of **urate oxidase** during the evolution of hominoids could be caused by two independent events after the divergence of the gibbon lineage; the nonsense **mutation** at codon position 33 resulted in the loss of **urate oxidase** activity in the human, chimpanzee, and orangutan, whereas the 13-bp deletion was responsible for the **urate oxidase** deficiency in the gibbon. Because the disruption of a functional gene by independent events in two different evolutionary lineages is unlikely to occur on a chance basis, our data favor the hypothesis that the loss of **urate oxidase** may have evolutionary advantages.

L17 ANSWER 9 OF 40 MEDLINE on STN
ACCESSION NUMBER: 90386634 MEDLINE
DOCUMENT NUMBER: 90386634 PubMed ID: 2403354
TITLE: Human **urate oxidase** gene: cloning and partial sequence analysis reveal a stop codon within the fifth exon.
AUTHOR: Yeldandi A V; Wang X D; Alvares K; Kumar S; Rao M S; Reddy J K
CORPORATE SOURCE: Department of Pathology, Northwestern University Medical School, Chicago, IL 60611.
CONTRACT NUMBER: R37 GM23750 (NIGMS)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1990 Sep 14) 171 (2) 641-6. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M30291; GENBANK-M30292; GENBANK-M30293; GENBANK-M30294
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901019

AB Using the cDNA and selected genomic probes of rat **urate oxidase**, we have screened the human genomic library and isolated seven clones; one clone (clone 13) contained exonic regions which

correspond to the exons 5, 6, and 7 of rat **urate oxidase** gene. The nucleotide sequence was determined for these three exons and exon/intron junctions, and compared with the sequence from the rat gene. A **mutation** resulting in a stop codon TGA was found in the fifth exon of the human **urate oxidase** gene. Sequence analysis of the polymerase chain reaction amplified **DNA**, corresponding to the fifth exon of **urate oxidase** from **DNA** samples from four different individuals, confirmed the same TGA stop codon in all. This single stop codon **mutation** and/or other **mutation**(s) in this gene may be responsible for the lack of **urate oxidase** activity in the human.

L17 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:493718 CAPLUS
DOCUMENT NUMBER: 119:93718
TITLE: Cloning and expression of **uricase** gene of Cellulomonas
INVENTOR(S): Yagasaki, Makoto; Ishino, Shuichi; Iwata, Kazuhisa; Azuma, Masaki; Teshiba, Sadao; Hasegawa, Masaru; Yamaguchi, Kazuo; Yano, Keiichi; Yokoo, Yoshiharu; Hashimoto, Yukio
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 545688	A2	19930609	EP 1992-311004	19921202
EP 545688	A3	19940105		
EP 545688	B1	19980408		
R: DE, FR, GB, IT				
JP 06038766	A2	19940215	JP 1991-320525	19911204
JP 2971218	B2	19991102		
CA 2084384	AA	19930605	CA 1992-2084384	19921202
CA 2084384	C	20020604		
US 5376545	A	19941227	US 1992-985690	19921203

PRIORITY APPLN. INFO.: JP 1991-320525 A 19911204
AB The **uricase** gene of C. flavigena is cloned and expressed in a host cell, e.g. Escherichia coli.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	180.08	180.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.11	-9.11

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 5, 2003 (20030905/UP).

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION

FULL ESTIMATED COST	0.72	181.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.11

STN INTERNATIONAL LOGOFF AT 11:41:13 ON 10 SEP 2003

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=> file medline caplus biosis
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:45:55 ON 10 SEP 2003

FILE 'CAPLUS' ENTERED AT 11:45:55 ON 10 SEP 2003
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FILE 'BIOSIS' ENTERED AT 11:45:55 ON 10 SEP 2003
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=> s sus scrofa
L1          3277 SUS SCROFA

=> s (sus scrofa or porcine)
L2        124180 (SUS SCROFA OR PORCINE)

=> d l1 ibib ab

L1   ANSWER 1 OF 3277      MEDLINE on STN
ACCESSION NUMBER:    2003394609      IN-PROCESS
DOCUMENT NUMBER:     22812702    PubMed ID: 12931905
TITLE:               Phytase, high-available-phosphorus corn, and storage
                     effects on phosphorus levels in pig excreta.
AUTHOR:              Baxter Christopher A; Joern Brad C; Ragland Darryl; Sands
                     Jason S; Adeola Olayiwola
CORPORATE SOURCE:    Dep. of Agronomy, Purdue Univ., West Lafayette, IN 47907,
                     USA.
SOURCE:              JOURNAL OF ENVIRONMENTAL QUALITY, (2003 Jul-Aug) 32 (4)
                     1481-9.
                     Journal code: 0330666. ISSN: 0047-2425.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 20030823
                     Last Updated on STN: 20030823
AB   Phosphorus-based land application limits for manure have increased the
     importance of optimizing diet P management and accurately characterizing
     the bioavailability of manure P.  We examined the effects of pig (
     Sus scrofa) diets formulated with high-available-P corn
     and phytase on P levels in excreta and slurry stored for 30, 60, 90, 120,
     and 150 d.  Twenty-four pigs (approximately 14 kg each) were fed one of
     four low-P diets: (i) normal corn, no phytase (control); (ii) normal corn
     with 600 phytase units kg(-1) (PHY); (iii) high-available-P corn, no
     phytase (HAP); and (iv) high-available-P corn with 600 phytase units
     kg(-1) (HAP + PHY).  Fresh fecal and stored slurry dry matter (DM) was
     analyzed for total phosphorus (TP), dissolved molybdate-reactive
     phosphorus (DRP), dissolved organic phosphorus (DOP), acid-soluble
     reactive phosphorus (ASRP), acid-soluble organic phosphorus (ASOP), and
     phytate phosphorus (PAP).  The PHY, HAP, and HAP + PHY diets significantly
     (alpha = 0.05) decreased fecal TP 19, 17, and 40%, respectively, compared
     with the control.  Dissolved reactive P was 36% lower in the HAP + PHY
     diet compared with the other diets.  Relative fractions (percent of TP) of
     DRP, DOP, ASOP, and PAP in slurry generally decreased with storage time up
     to 150 d, with the largest decreases occurring within 60 to 90 d.
     Diet-induced differences in relative fractions of DRP, DOP, ASRP, and PAP
     were significant when averaged across storage times, simulating a
     mixed-age slurry.  Relative fractions of DRP in simulated mixed-age
     slurries were higher in HAP and HAP + PHY diets, indicating that diet may
     affect P losses under certain P-based application scenarios.
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=> s papio hamadryas
L3         1462 PAPIO HAMADRYAS

=> d l3

L3   ANSWER 1 OF 1462     MEDLINE on STN
AN   2003326898      IN-PROCESS
DN   22740447    PubMed ID: 12856792
TI   Numerity of a socially housed hamadryas baboon (Papio
     hamadryas) and a socially housed squirrel monkey (Saimiri
     sciureus).
AU   Smith Brian R; Piel Alexander K; Candland Douglas K
CS   Program in Animal Behavior, Bucknell University, Lewisburg, Pennsylvania
     17837, USA.. brian_r_smith_333@hotmail.com
SO   JOURNAL OF COMPARATIVE PSYCHOLOGY, (2003 Jun) 117 (2) 217-25.
     Journal code: 8309850. ISSN: 0735-7036.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   IN-PROCESS; NONINDEXED; Priority Journals
ED   Entered STN: 20030715
     Last Updated on STN: 20030715


=> log
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                14.44      14.65

STN INTERNATIONAL LOGOFF AT 11:48:02 ON 10 SEP 2003
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WEST Search History

DATE: Wednesday, September 10, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L11	dna and uricase.clm.	32	L11
L10	dna uricase.clm.	0	L10
L9	recombinant uricase.clm.	0	L9
L8	uricase and (97 or 291 or 301).clm.	18	L8
L7	uricase and (97 or 291 or 301) and dna.clm.	31	L7
L6	L5 and dna	175	L6
L5	uricase and (97 or 291 or 301)	337	L5
L4	urate oxidase and aggregate	24	L4
L3	urate oxidase and aggregate free	0	L3
L2	urate oxidase.clm.	19	L2
L1	(urate oxidase.clm.) AnD ((@pd > 20030908)!)	0	L1

END OF SEARCH HISTORY